Hadlow, William 2004

Dr. William Hadlow Oral History 2004

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NOTE: Not all names and places were able to be verified.

Dr. William Hadlow Interview

Office of NIH History Oral History Program

Interviewer: Maya Ponte

Interviewee: Dr. William Hadlow

Transcript Date: August 31, 2004

[*Beginning of transcript]*

Interviewer: I spoke with Bruce [Chesebro] this morning.

William Hadlow: Byron said he would be away.

Interviewer: Yeah Byron is away, but I will speak with him some time over the phone probably. I mean, I've actually spoken with him at meetings.

WH: He said he had met you, yes.

Interviewer: Yeah. Oh, okay that's nice. Okay that was very nice of him to mention.

WH: Yeah I talked with him.

Interviewer: Yeah I like Byron. He's a great guy.

WH: Yes, I [unintelligible] discuss science with him but I see now on the outside.

Interviewer: Right. Can we start actually if it is okay with you can we start with Carl Eklund and sort of your relationship with him. How it began, how it evolved.

WH: Well when I was at the University of Minnesota, in graduate school at the new school of veterinarian medicine, I came there are an instructor of veterinary pathology. That was a big change because when I graduated from veterinary college in March of 1948 [from Ohio State University] I was going to go into the dairy cattle practice in Cortland, New York. I'd worked with a practitioner up there. Anyway, Jay Sauter whom I've known when he was in school at Ohio, he was a couple of classes ahead of me. I lost out about three years because I quit and joined the navy, but anyway he persuaded me to come up there for graduate work. And so I was up there and I forget just when it was Carl Eklund, I didn't know Carl Eklund, but he came through there and he always came over to the veterinarian school to talk with people there. At that time he was spending essentially all of his time studying Western encephalomyelitis virus. It was a big study. Well, Western and St. Louis and he would tell us about it. Well, I didn't know anything about Carl Eklund and didn't know anything about Rocky Mountain lab, but so that was I think my first meeting with Carl. He may have stopped there several times. Anyway, later, I went over to the medical school. I spent three years there in pathology and he came looking for me.

Interviewer: Oh my gosh, so you must have made an impression on him.

WH: It was early – it was either late 1951 or early 1952 and at the time I was working in Austin, Minnesota at the Hormel Institute, which was part of the graduate program, and George Young was working on a pig disease there which eventually was called Transmissible Gastroenteritis of piglets. I forget what kind of a virus that is, but anyway, I was down there when Carl came and someone who had spent some time here at Rocky Mountain lab and knew Carl Eklund had spoken with him when he was looking for me and he conveyed the message to me that Carl was looking for me for a job out here. So I was running out of support for my graduate study anyway, and my advisor was James Dawson of Dawson's encephalitis, he was head of pathology at the medical school. He wanted me to stay there. In the end had in mind that he would encourage me to go into medicine, but I was running out of support. I had exhausted all of the avenues I had for support, and so I was looking for a job. Well I got in touch with the people out here at Rocky Mountain lab and a man that I knew in the graduate school that told me about Dr. Eklund looking for me told me a little bit about Rocky Mountain lab. Otherwise I didn't know anything about it. So I –

Interviewer: What did he tell you? What did he tell you about the lab?

WH: Oh, that at that time the emphasis was on diseases of nature transmissible to man. So a lot of field work and he described the director Carl Larson sitting up in his office with a pair of boots on that sort of –

Interviewer: So a real outdoors man?

WH: Anyway I was accepted. I don't remember the details. I may have it somewhere. I was accepted. Apparently what happened they did have a pathologist here, Jack Frankel who made his name with toxoplasmosis. He left here I think and went to the University of Kansas and so the position was open for about 18 months and they were going to lose it unless they filled it and in the interim people like Carl Eklund, Bill Jellison, thought they ought to have a veterinarian pathologist instead of an M.D. pathologist. So that's the reason Carl came looking for me and I got the job.

Interviewer: So they didn't have a veterinarian pathologist here at the time?

WH: No.

Interviewer: No, okay.

WH: There were three veterinarians here who were sort of seconded and are not really part of the permanent staff. They were sent here from CDC. They were part of the Jim Steel's public health veterinarian group; Herb Stoenner, Carl Reinhard, Laurie Luoto. Luoto was down in Los Angles County studying Q fever. Reinhard was here and I worked with him. He was working on leptospirosis in dogs and cattle and Stoenner was – I don' t know what he was working on. I was the only veterinarian pathologist. It was really a challenge to come out here become acquainted with all the diseases they were working on. They were totally unfamiliar to me; *psittacosis* plague tularemia, Rocky Mountain spotted fever –

Interviewer: Were they exciting or did it seem interesting?

WH: Oh yes, it was a real excitement.

Interviewer: Yeah, I can imagine.

WH: I was on my own and I was given a lot of support. Carl Larson the M.D., the director, gave me wholehearted support and I was certainly green.

Interviewer: And when you say you were on your own were you working with other people at the institute or how…?

WH: I had my own lab here. I was assigned to Dr. David Lackman who was the – at that time we had a resident director and the organization at the lab was in sections and I was assigned to the section of serology and pathology under Dave Lackman, and he led me around by the hand. He had to. It was just the ways of doing things, the government reports and all that nonsense.

Interviewer: Was it difficult coming from an academic setting? Did it seem like a lot of paper work…?

WH: Well not really.

Interviewer: No?

WH: Well it was the usual annual reports or quarterly reports, but Dave helped me with that. Otherwise I was given a lab and there was a technician here who was a holdover from when Frankel was here. He didn't last long. He got into some problem here at the lab and then I inherited a man who worked with me for 20 years. I trained him as a histo-tech.

Interviewer: And who is this?

WH: It was Clarence Robinson.

Interviewer: Okay.

WH: His wife is still here. She comes up here sometimes. He had been working in the yellow fever vaccine unit, and during the war they made the vaccine for the military here, and that was being disbanded and in the fall of 1952 they completely disbanded that unit and that whole building is gone now. They talked about preserving some of the old buildings well they tore the one down that had the most significance. That's where they made the vaccine and that's where Carl Eklund found the poliovirus and the cutter vaccine.

Interviewer: Yeah, well that's a fascinating story too.

WH: That's an interesting story too.

Interviewer: Yeah.

WH: But anyway Clarence Robinson, then, was assigned to me about the first of the year of 1953. I trained him as a histo-tech and he turned out beautiful material. I had a lot of people comment on that and he always pleased me because he did it my way. He didn't know any other way. But he worked with me for 20 years; we turned out beautiful stuff and –

Interviewer: And when you say he did it your way are there many different ways you can do the sectioning and the staining of tissues?

WH: Staining, different stains and –

Interviewer: So you developed preferences for using certain types of stains?

WH: Yeah. The way you put the section on the slide. You don't have to do this to look at it. It's already –

Interviewer: So you don't have to crane your neck –

WH: The way it's supposed to be.

Interviewer: Okay, so sort of the layout? Like it should be a chemical –

WH: Take it out of the water bath and put it on a slide. Anyway, but I had a lot to learn and at that time a lot of animals were used here and that was one of the nice features of Rocky Mountain lab you had a lot of experimental animals and admittedly the constraints on using experimental animals were far less than there are today, but they were handy. You didn't have to go out a few miles to a farm where they were. They were right here.

Interviewer: So what kind of experimental animals did you have at the facility?

WH: At that time they had a mouse colony, a Swiss mouse that they originally brought out here because they were useful in working with the yellow fever virus. So they had a mouse house, and that was quite an operation, and they raised guinea pigs and when I came this Carl Reinhard, one of the veterinarians from CDC, they built kennels, outdoor kennels for beagle dogs and he was using those – they were breeding beagle dogs and he was using those dogs on his experiments for leptospirosis. So there were still a few of those around although his work leptospirosis with dogs had been terminated and he was then working on leptospirosis in cattle and I worked with him on that and that was all they had, maybe a horse out back and they had a number of cattle around.

Interviewer: Did they? Like on actual –

WH: They were right there.

Interviewer: Really?

WH: Oh yeah. That whole meadow out here we used to raise hay on and it's all gone now.

Interviewer: So you raised hay to feed the animals. You kept cattle. Were there sheep?

WH: Yeah. We don't know whether they had sheep at that time, but they may have had a horse around –

Interviewer: So they had a barn? Like a livestock –

WH: Well they had some sheds there and stock of paddock, and that was fairly close up – I think about where that BL3 building sits. Anyway, so they had a few cattle and they were left over from Dr. Stoenner's study on Q fever in cattle and there were quite a few of them out there in the pasture. So those animals were left, but in running this and trying to become a pathologist I had all this stuff and I would – I was monitoring the mouse colony for indigenous diseases and there were a number of things, because it had a bearing on – most people forget that. You get a mouse to use experimentally, especially a pathologist and he looks at some sections and he sees something, well if you look enough of the normal you get the background –

Interviewer: So for instance there could be a background infectious –

WH: Yeah we call it the background static.

Interviewer: – disease or something in the mouse colony?

WH: That's right.

Interviewer: So if you're not familiar with what's there then you –

WH: Oh I found a number of things. We had Tyzzer's disease and they had chronic pulmonary disease of mice and rats, and well I looked at a lot of mice. So that was my way of learning something about mouse pathology and then, at that time as I mentioned, we did a lot of fieldwork. So there was always – I was always sort of brought in – dragged in by Bill Jellison. He's one of the old time naturalists.

Interviewer: What was his position here?

WH: He was a parasitologist. I think his specialty in that area was fleas, but he had a wide interest in diseases of wildlife. Didn't have any real background in pathology but we worked together so all that material came in another [unintelligible].

Interviewer: So when you say he was a naturalist what do you mean?

WH: He would go out in the field. He could identify all the animals, all the plants and give you a whole picture of the ecology and he grew up that way and you don't find too many of them with that kind of broad interest, but I'm going on and on.

Interviewer: Oh no that's really interesting. So he would bring in samples from the community?

WH: Yeah. In fact one time he had a moose up on the second floor on a table like that doing a post mortem. I said, "What are you doing?" "Oh, I had to get a decent post mortem on animals" and the back of – well we called building 5. It's the south wing clear at the end where they attached the new part to it; most of those rooms down there were built for housing large animals when they were studying encephalomyelitis. I took the end room, and it happened to be the directors animal room, but he – and he had willingly gave it up so I could get – because I wanted a place where I could bring a cow in or a horse and do a post mortem. I was working on mice and the fixed that up. So, I looked at cattle a lot of calves. A lot of this I was doing on my own because I was interested in trying to become a veterinary pathologist, because I really didn't have any professor. My mentor was a Scotsman that I contacted. He was on the East coast.

Interviewer: Who was that?

WH: JRM Innes, and he was of the old school. He got most of his pathology training in Germany and he left Britain in 1948. I think he was a little too critical of what veterinary pathology was like in the U.K. at the time and it made him uncomfortable – or they made him uncomfortable so he came to live and work in the United States and I contacted him by letter in response to something that he had written. You know back then in the 1950 – 1949 /1950 there was very few places you could go and get good training in veterinary pathology and, in fact, the whole specialty of veterinary pathology wasn't really developed to the extent that it needed to be, and he was promoting that. Well, I had wrote to him and got a nice letter back from him. We exchanged a lot of letters and ours was epistolary arrangement. He typed both black and red part of the ribbon, write up the side and down, and he always signed it Hamish, Scottish for Jim, Hamish. Several years later I met him at the Armed Forces Institute of Pathology in one of their short courses and we just hit it off. He was really my mentor. He gave me the sort of good advice and encouragement that I was looking for out here on my own trying to –

Interviewer: So he was like a long distance mentor?

WH: It was a long distance –

Interviewer: And it was all through letters? Like all through exchange of letters?

WH: Mostly through letters and then we had occasional meetings. We wound up – he was working at Edgewood Arsenal and then he worked out on Long Island and I stayed with him once in Baltimore and then I was on Long Island. So I used to see him and his wife Margery fairly often.

Interviewer: So how – so when you had issues I mean you were basically teaching yourself –

WH: That's right.

Interviewer: How to do veterinary pathology. I assume you had some textbooks and some something to go on.

WH: There were very few textbooks.

Interviewer: Very few…

WH: There was only one textbook.

Interviewer: Because to me that seems like such a daunting task when – I mean it's hard enough when you do medical pathology when you're dealing with one species and you're talking about how does sheep, mice, etc.

WH: Anywhere from a mouse to a moose.

Interviewer: I mean to me that's just amazing so there must be – what is it like – how do you teach yourself to back and forth between something as –

WH: You have to be aware of the species differences and the way they respond. That's the challenge and that's the –

Interviewer: So when you had a question of a difficulty who – would you write a letter or how would you…?

WH: I'd get in touch with Dr. Innes, because he had broad experience and in those days it was all anatomical, morphology and that sort of thing, having had experience in morphology. Well anyway it was a challenge, but there were all of these animals being brought in and I was sort of the village pathologist. Farmers' wives would drag in chickens and, well, I did it – I had the freedom to do it for one thing. No one ever told me what to do. I was singularly fortunate. No one ever told me what to do. I just did it and apparently satisfied them with my annual report that indicated that I was doing something, but whatever I could diagnosis. Poultry pathology is quite complex, but I could diagnosis them with a post mortem. There was a lot of tuberculosis and leucosis. I could diagnosis that with a necropsy, and then some interesting viral infections of chicks and even nutritional vitamin E deficiency, crazy chickens and things like that. Oh yeah, I did that and then I looked a lot of calves and lambs because at that time the big problem here was a selenium deficiency producing a myopathy.

Interviewer: Is that because of the soil conditions here?

WH: Hmm.

Interviewer: Okay.

WH: And I had this interest in neuropathology that I developed when I was in graduate school and tried to become half way adept at evaluating changes in the nervous system and I went looking at a lot of horse brains that the practitioners would bring in.

Interviewer: This is so interesting. How did this – what kind of relationship with all of this work that you were sort of doing for the community what sort of relationship did you develop with the community? Did people know you?

WH: Oh yes in those days it was quite different. I'm talking about the way things were 50 years ago in Hamilton. Population for Ravalli County in the valley was somewhat less than 13,000, now it is 38,000. Everybody on Main Street is a stranger. When I came here this was the new guy on the block. Everybody knew I was – who I was. I just came here, so it was quite different, and the lab had a more familial air to it.

Interviewer: I was wondering about that. What was the relationship like between the lab and the community at that time?

WH: Well they didn't – it was set off here. They didn't really know what was going on, but it was a tic lab and I think if the administration were to be faulted at that time is they didn't have any P.R., very little, but everybody knew us. [for example they would say] Oh, he works up there in the lab and –

Interviewer: How did they find out that you were the man to bring the sick or the dead animals to?

WH: Well it got around and I had my contacts with the local veterinarians. I even looked at some human material, because I knew the few physicians we had at the time. I remember looking at a herpes simplex encephalitis that hits the temporal lobe in the brain, I knew – got to know a lot of wildlife biologists, mainly through Jellison. He had contacts, and another person that worked at the lab, an M.D., Fritz Bell [J. Fredrick Bell], spent a lot of his time in the later years on rabies and Don Lodmell worked with him that's what he got his doctorate in, and Fritz had a lot of contact with wildlife people, biologists, at the university in the department of zoology.

Interviewer: At the university in…?

WH: In Missoula.

Interviewer: In Missoula.

WH: Hmm, mmm.

Interviewer: So you had contacts there all the way there as well.

WH: Yeah. I remember going down there once showing – demonstrating to some of their wildlife students how to do a necropsy on a deer. This was back on a loading dock of one the buildings. So I had those contacts, but it was great for me trying to be a veterinary pathologist. I had gotten all of this varied experience.

Interviewer: It seems incredible because you were able to draw on not only like livestock and sort of agricultural animals, but also this whole wildlife side –

WH: Yeah and all the lab –

Interviewer: Natural…

WH: All the material used looking at 7 day old mice, suckling mice and then, of course, I got into a lot of primate work, monkeys with Carl Eklund on polio.

Interviewer: So tell me about that. I mean I know this is a little bit of a diversion, but I actually think this is really interesting. How did he figure out or who figured out that the vaccine had to live?

WH: Well and to go back to Carl Eklund, when I first came here I didn't have any working relationship with him, but then I did look at some of his material. The suckling mice they used to demonstrate Colorado tick fever virus and it produced some interesting lesions in the brain and I had a way of looking at mice. There was a big project here also at the time that involved looking at these mice. By the time I got them they were maybe 7 days old with coxsackie viruses and I looked at a lot of mice, because in those days they used to separate the A group from the B group-- coxsackie viruses on the basis of the lesion – the pattern of lesions in these mice. I had a way of cutting up a baby mouse that was maybe that long into 7 sections just like that and you could see every organ that way. And I did a lot of that with Eklund.

Interviewer: So this was sort of a technique that you had developed for being able to very nicely visualize what was happening inside of these mice.

WH: Yeah – it was the level that you cut. You knew with this section you'd see kidneys, this one spleen and liver, and so forth.

Interviewer: And that was something that Carl found helpful? I mean that was – or in studying – in doing the research that they working on.

WH: Well he encouraged me to continue to do that. I was looking at a few and a lot of things I'd just collected mainly because I wanted to see what was happening. No one had been being doing any pathology. That was – they'd use an experimental animal and produce some kind of disease and that served their purpose and then it was chucked out, but I was interesting in what had taken place. So I looked at all kinds of stuff, looked at guinea pig scrotums because that was the diagnostic change in spotted fever.

Interviewer: Oh interesting.

WH: That was standard. I wanted to see what was going on in the tunicate and all that stuff so anyway I did that, but it was – when I first started working with Carl, then, it was in about April of 1955, someone called him and told him about what was happening in Idaho. That was down around Pocatello when they were just starting to use the Salk vaccine and low and behold some of the kids were getting polio and the virus was getting out and parents – parents were coming down with polio. That's all Eklund needed he ran out and he was gone for two weeks. That's another whole story. I don't get into it because I think in the end he got his knuckles rapped for – well, there's some political stuff and that.

Interviewer: For being a maverick instead of collecting the samples himself –

WH: And you know going over the heads of people. He just went out on his own.

Interviewer: Right he wanted to get to the heart of the problem. He didn't want to deal with the bureaucracy, yeah.

WH: And it cast poor light on some of the people back at NIH, because these vaccines had passed the safety test. Well anyway that's another whole story.

Interviewer: Sure.

WH: So he was gone and Carl was of the old mode physician; he would do the lab side of it. So when he went out he would do his own neurologic exam, the whole clinical exam, and even do his own autopsies. He grew up that way in Minnesota at the time when he went to medical school, and so he brought back all kinds of stuff. He brought back some human brains, well other tissues, the vaccine, and they said that there's got to be a viable virus in that vaccine. I don't remember the details but we got all of these monkeys and that's another whole story too, getting monkeys back at that time they came directly from India or the Philippines or – that was another whole thing. Got into a lot of interesting intercurrent diseases with these monkeys – a lot of tuberculosis.

Interviewer: Because from transporting them, probably, two together –

WH: Lesions…and then this one that causes gastric adenomas [unintelligible].

Interviewer: So there was – there were complications with using the primate model system, because –

WH: You had to aware of it, yeah.

Interviewer: There were all kinds of intercurrent diseases.

WH: You had to be aware of it. Anyway Carl inoculated monkeys that were cynomolgus and rhesus [unintelligible]. I think originally he put it correctly into the spinal cord, used the vaccine right on the spinal cord. In a few monkeys I think he and I'd have to look at the nodes and treated them with cortisone. Anyway, lo and behold they developed paralytic polio.

Interviewer: Even the ones not treated with cortisone?

WH: Yeah.

Interviewer: Yeah.

WH: So I had – immediately had a great experience looking at monkeys with polio.

Interviewer: That's incredible.

WH: Some days I'd do 10 post mortem just like that on all of these monkeys and well all those satellites to that too, but anyway Carl demonstrated that it was viral – poliovirus in the Salk vaccine that had been prepared at the Cutter laboratory in California. Well that's –

Interviewer: But so there were people who really didn't want this to be known, was that part of the problem?

WH: Well, I think they wanted it dealt with differently because the vaccine had passed the safety test.

Interviewer: Right so it became an embarrassment for some of the…

WH: Well after having looked at all those brains and cords from Carl Eklund's monkeys I think I had pretty good idea of what polio was like, and I looked at a couple of these human things that he brought back and I had –

Interviewer: Were they fairly similar looking at the –

WH: Essential lesions were the same. It was inflammatory and it knocks out neurons and I looked at some when I was taking neuropathology in Minnesota and I knew the human brain because that's where I learned more anatomy, when I had to dissect the human brain. Well in those days I said they had polio. Well somebody's got to prove that it was polio, how to know what polio looks like in a monkey. In those days there was a fellow at John Hopkins. What the devil was his name? Anyway he was the one that setup the protocol for the proper way of looking at the brains and spinal cords of the monkeys that were used in the safety test, and you literally had to account for every little black dot in the section.

Interviewer: Oh geez, so it wasn't Richard Johnson or someone like?

WH: Hmm?

Interviewer: I'm trying to think of who at John Hopkins –

WH: No it wasn't Dick no. This was –

Interviewer: This is before Dick?

WH: This fellow was actually, he was actually an anatomist. His name will come to me. No Dick was a good friend who came later. So anyway I was – I had to go back to NIH to learn how to do this. So in the fall of 1955 my wife and I went back to Bethesda and I was assigned to L.L. Ashburn, a great Virginia gentlemen. He was at the Institute of Arthritis and Metabolic Diseases I think it was called, and he worked under Ralph Lillie who was the pathologist for NIH. Ralph Lillie, he was still there, and Lou Ashburn worked under him. Well Lou was in charge of people that were doing the safety test – just looking at the material and –

Interviewer: Wait doing the safety tests for the vaccines

WH: Yeah.

Interviewer: At NIH? Like the people who should have caught the Cutter thing?

WH: Well I guess they did. It just happened – they didn't miss it I'm sure, but for other reasons that came to light the particular tests that were done, I'm sure they were negative.

Interviewer: So they were testing them post going on market? Is that the – was that the issue?

WH: Yeah, and then I think in the end, I don't know how they really explained it, except that maybe some packets of virus just weren't left vulnerable to the formaldehyde that was being used and it got slipped through and then you got how often that happened? I don't think it was ever demonstrated, but certainly the vaccine that Carl brought back that had been used on [?] children did have viable polio virus, and then others did I think demonstrated that too. Jerome Severton [spelled phonetically] was at the University of Minnesota at the time and he was the head of microbiology and rickettesiology. He was a tough guy, but he was one of old-timers in virology. Knew what he was doing and I think he demonstrated it, too, by inoculating.

Well I went back to NIH and Lou said, "Hell, [?] you don't you have to spend your time looking at any monkey material here. I know that you've looked at a lot out there," and at that time he was doing all the pathology for the marine hospital. So they sent in surgical material, necropsy material and he had – there were about four residents that worked under him, and he put me in with them. I was back doing what I was doing in Minnesota, looking at all that stuff and you had the – you got the material and you had to describe it and so forth, get the sections cut, and make your diagnosis and then take it to him, because he had to sign off on it.

Interviewer: Right so you were back to doing the pathology resident's job of hospital diagnosis.

WH: And there were – Louis Sokoloff [?] was there. He made his name as an arthritis pathologist.

Interviewer: So were you upset at being put in that position or were you – how did you feel?

WH: Lou was a great fellow to work with.

Interviewer: Okay.

WH: Yeah and these M.D.s that I worked with – trying to think of the name of one who was always after me to bring him some elk steaks. But what was his…? I can't think of his name. I had a good time back there. So I was there and doing that with Lou Ashburn for several months, and then I went to AFIP and was assigned to Webb Haymaker's section of neural pathology and he said, "How long are you going to stay?" I said, "Well they've given me a month." "Oh, I thought you were coming for a year." Well that would have been great working with him, but he was there. He was gone most of the time. So and there was a retired naval – he wasn't retired, there was a naval – a captain in the naval medical corps a pathologist. He looked like Charles Laughton. You know I can't remember his last name, but he was there most of the time and he was an old time neural pathologist and I looked at a lot of – it was all human material, but it was great working with him.

Interviewer: So did you feel like you learned a lot during this period?

WH: Oh yes. Oh yes.

Interviewer: Okay.

WH: I was learning all the time, yeah and then when Webb Haymaker was there we had sack lunches and you knew you were going to be grilled in some aspect of neural anatomy. Well then I spent a month in the veterinary section with Thomas Carlyle Jones, that was a good connection. Well that was the polio story. I've gone on too much about that.

Interviewer: No that's – I mean but that is interesting. So wait you worked there then – so you finally then did go back to polio when you went and worked and with Charles?

WH: When I worked with…?

Interviewer: What was his name? The person – you just said when you back to the veterinary section for a month.

WH: Oh with Jones?

Interviewer: Jones, yeah.

WH: Well that was all veterinary; there wasn't any polio, but it was a good experience because that was the Mecca AFIP is the Mecca for pathology, medical and veterinary alike.

Interviewer: So did you get to polio at all while you were there?

WH: Nope.

Interviewer: They sent you back to make sure you knew polio and you completely did for other stuff –

WH: Yeah that was Lou Ashburn he said, "You don't have to do that." I think I went over to see – I may have looked at a few sections – there was a tall veterinary pathologist there at the time by the name of Loomis [spelled phonetically] working under Lou Ashburn and he was doing a lot of his monkey work. I may have looked at a few of his sections, but it was probably something else, some other lesion that he was showing me.

It was all gallbladders from then on – at that time the Indian Health Service went through the marine hospital so we got a lot of material from the American Indians, and it was stuff that I had been exposed to at Minnesota, the usual stuff. A lot of skin wedges and what not. So anyway we came back…

Interviewer: Back to Rocky Mountain?

WH: April of 1956 and then it was in 1950 – the spring of 1958 in February / March we went to England.

Interviewer: Okay how – what happened – what was critical that happened then that caused the USDA to want to send you to England and how did they pick you?

WH: I was contacted – my wife and I were living out of town, [south of the city of Hamilton on Blood Lane, named after the Blood family] on a chicken ranch – chicken – it was a chicken ranch and it must have been in, I don't know May or June of 1957. In 1957 I had a letter from the USDA saying they were looking for someone to work with the British on scrapie and I knew scrapie had occurred in this country. It had first appeared in 1947, but then in 19 – about 1950 there were more cases and so they got excited and they had an eradication program and they didn't facilities to – they didn't want to work on scrapie in this country because of tight controls over – I don't know what it is like now, but in those days it was tight control and even sending a section of brain was hard…they said that they had had –

Interviewer: Tight controls on working with scrapie tissues in lab?

WH: I don't know what their controls are here, but when I worked out on it was highly controlled by USDA. I think they said in the letter that they had had difficulty convincing – persuading others to take others to take this position and at that time you were either to be assigned to the agricultural research council field station at Compton in Berkshire or at the Moredun Institute in Edinburgh. I just assumed that I was the last one on the list. I don't the names of the others that they had contacted, but I was the last on the list and well I had – I don't know whether restive is the word, but I had been at Rocky Mountain lab it had been about six years and I wasn't in the Commission Corps, all the other veterinarians were. I was just straight Civil Service and I didn't know whether I was – well I wasn't certain that I wanted to make a career in the public health service as a veterinarian. I was really actually thinking more about going back to academia. I wanted to get into a veterinary school. Anyway I was – they called at a time when I was probably more receptive to such an offer. So I talked it over with me wife and decided – we decided we would go. So that was June '57 and then we left I think February ' 58.

Interviewer: Did you have a choice between Compton?

WH: No I didn't. In the end I didn't. I was wound up at Compton, which was probably the better place at the time. So I went to Compton and William Gordon [W.S. Gordon] was the director, a tough Scotsman from Ayrshire, and in those days most of the veterinary labs, I think even some of the medical labs, were run by Scotsmen. I think their administrative ability and other things were a little better than some of the Englishmen. Anyway Bill Gordon was great. So he was concerned, he thought that I was virologist when I came, but I said "No I'm not I'm not a virologist. They said you needed a pathologist." He said, "Well we've got Pattison [Iain H. Pattison]." I said, "Well okay." So he assigned me to Pattison and I said, "Well I'm not a virologist but I will help out in pathology." So he says, "Okay and then he let me do what I wanted to do." He assigned the best histo-technologist there, Peter Dennis and he turned out beautiful material. I still have it I should put somewhere because it's great stuff. He used to cut whole sections of sheep brain, and anyway we got beautiful material. So I was assigned to Iain Pattison who was a fellow Scotsman, but he was from Abriachan.

Interviewer: What was he like?

WH: Very much the gentleman always well dressed, smoked quite a bit, well they all did in those days, but very much of a gentleman, a kindly person and he was pleasant to work with. He didn't bother me; let me do my thing.

Interviewer: Were you attached to his laboratory?

WH: Not really. His lab was up in what they called the isolation compound, which was, I don't know, how many acres where they had building to isolate large animals and you had to go through a foot bath and all that stuff.

Interviewer: To make sure that you're not transmitting the disease.

WH: I was assigned to or they gave me quarters in a building called the pigeon house.

Interviewer: Why did they call it that?

WH: And it was – it actually had been used as a pigeon loft and they had an outbreak of ornithosis, psittacosis, so they depopulated the whole thing and then I don't know how long after that they repopulated it with this motley crew including an American. And so facilities there were lofts with sliding doors. It was up by itself on the hill, a lot of nice of flowers around.

Interviewer: That's nice. I've been to Compton –

WH: Have you?

Interviewer: I know what it looks like.

WH: Oh the pigeon house is probably gone.

Interviewer: It's probably gone, but it's just gorgeous. I love – I mean just love the whole the rolling hillsides and…

WH: They didn't have all that behind it then. They do now I guess. I was there – the last time I was there was in '86, but so I was assigned there and I used to go with Pattison every Monday morning, put on your boots and your boiler suit and this big heavy rain coat to go up to the isolation compound and look at all the animals. They had hundreds of sheep and goats up there. You would go into some of these pens, oh they might have 30 animals in there, six of them or more would have scrapie, various stages of scrapie. All kinds of material and I was just salvaging that, because they were used for some other experiment. I couldn't do experiments myself because I didn't have the permit. I had to have a permit to inoculate a mouse from the Home Office, and I did inoculate goats with Pattison's technique. It's the one that I used here and it is still better than the one that they require over here. That's a lot of nonsense that –

Interviewer: What's the technique that you use?

WH: You do it locally; you don't have to knock them out. I had a slick way of doing it. You put a sheep or a goat in – we had a cradle like they had in England. You know and they're in like that. You've got a man sitting here holding the head, clean up the area, do a little local, take a drill and drill through the calvaria barrier, just like that –

Interviewer: Seems much faster.

WH: Yeah, it was better, a little incision like that and you turn him loose and he's back eating.

Interviewer: So now they anesthetize – they do general anesthetic.

WH: I think the regulations require that you give them general. I don't like that. We did hundreds of them over there and I did plenty of them here without complications. I think over there we had there may have been a complication, a pituitary abscess or something. They never got meningitis or anything; we did it carefully.

Interviewer: Yeah I think I remember reading one study and I can't remember even what the object of the study was but just I remember them saying that they inoculated something like 100 or 200 animals within a like 24 hour period.

WH: Yeah he was running a marathon.

Interviewer: I mean these were large-scale inoculations.

WH: A lot of them are done in an intra-subcutaneous site where they could that much more quickly, but intracerebral inoculation; they usually want it here in the left parietal area. There's very little muscle, just so you got through the periosteum you were all right as far as the drill you had to cut through the periosteum so it didn't wrap up in the drill. No that was the quick way; we did a lot of them, but Pattison, he didn't bother me. We'd do those sessions and then I think he was interested in what I was doing. I never really discussed the details because his pathology of scrapie was quite different from mine. They just looked at through sections through the obex [unintelligible] part of the medulla for vacuolated nerve cells. Well it has the diagnostics but what's the brain like? Nobody ever looked. I was looking at everything and found all kinds of stuff…

Interviewer: Did that ever get published that work that you did?

WH: Yeah.

Interviewer: So the work you did at Compton from looking at the pathology?

WH: I don't have any reprints left.

Interviewer: Okay. No it's okay I can probably find it, but I just haven't seen that work.

WH: It was in the *Research in Veterinarian Science* for 1959, I think one on pathology of scrapie, experimental scrapie in the goat. I tried to make it into a doctoral dissertation, but they wouldn't take me at the University of London, because I wasn't a graduate; I couldn't do it off campus. There were others that were doing it there at Compton and no one at the University of Reading, which was close by, at that time could take me because they didn't know anything about the subject.

Interviewer: Geez. So you basically did dissertation quality work,

WH: Hmm, mmm.

Interviewer: But never got a dissertation, but never got a dissertation.

WH: Yeah.

Interviewer: Because I mean you characterized the histopathology in the goat of scrapie.

WH: Yeah.

Interviewer: Because here was Pattison, he was doing the inoculations and doing sort of the experimental end..

WH: Doing other studies, yeah.

Interviewer: Yeah. Interesting.

WH: He and his wife Margaret had two sons. One went on to be a physician Andrew and Mark a poultry veterinarian, but we used to spend a lot of evenings with them. He lived right there in Compton at that time and he was a great man to work with. And I last saw him when I took my son and daughter to England. We went out to Compton in 1986 and by that time he had moved to Newberry and we visited him. He'd had a heart attack and we went out in his garden and maybe a year or so later he died. He was always a gentleman.

Interviewer: Well it's good that you got to see him.

WH: Hmm?

Interviewer: I mean it's wonderful that you got to see him.

WH: My daughter and son had chance to meet him. They were a very gracious couple and the only time he got a little excited, as I remember, I was doing something on the scope manuscript in the flat in the kitchen of our flat, this old manor house, I stayed home that afternoon and Pattison came down there all excited. I kept a couple of animals up there much longer than they usually did, you know it was tight control, suppose they get scrapie.

Interviewer: Right because of the ethical sort of situation.

WH: Humane, I understand, but I wanted to push a few of these.

Interviewer: To get the histopathology, yeah.

WH: It was for my study. He says, "You've got a couple of animals up there. I know you're home off, but you'd better get up there because a woman from the Home Office coming, the inspector, and she has access to everything." If she had seen those animals that are in the late stages of scrapie, it looks pretty grim I think, so that was the only time he got a little excited.

Interviewer: Weren't there exceptions for when it was really – you know like there was a good reason to keep the animal alive, because you wanted to see what could happen to the brain?

WH: Well they didn't have that interest, and in fact they were all seasoned to this arrangement that you have to terminate these animals early for humane reasons.

Interviewer: I see so they were used to it and they didn't want to push any buttons or –

WH: No.

Interviewer: Make any make any waves?

WH: And they didn't have any reason to push them really to see how the disease played out clinically. They had probably seen enough from natural disease. So the experimental animals were usually terminated early, and so I probably shouldn't say this but some of them were lined up and passed for human food because the carcass was in good shape.

Interviewer: Right sure.

WH: I had a lot of help in the necropsy room supposedly. This was up in the isolation compound. It was actually run as sort of an abattoir and they had this--what was supposed to be the diener of the post mortem room. He was actually a wholesale butcher, a cockney, and I had a hell of time – old Mat you know he would speak a cockney dialect and after a while we could understand – I could understand him. He would – I would help him kill the animals. He killed them. We used electric tongs on sheep, so I didn't destroy the brain otherwise some of the larger animals there was a captive bolt –

Interviewer: Right, what mess.

WH: That'd mess up the – because a lot of the early BSE brains in Britain had been killed that way. It messes up, goes clear down to the thalamus.

Interviewer: Yeah that would really make it difficult to use them.

WH: But it was a good time there and W.S. Gordon and then, just down the hallway, was Dick Chandler.

Interviewer: So did you know Chandler –

WH: Oh yes.

Interviewer: While you were there?

WH: He had the flat above us. He and Angela had the flat above us and Dick would always hold – he would have séances up there. He was – Dick was great. He had a sense of humor –

Interviewer: What do you mean séances?

WH: I don't what – we were inviting in something from the past.

Interviewer: To help with the experiments or…?

WH: I don't remember the details of that. It was always kind of joke. I think he was chuckling on the side while he was doing it – had a great sense of humor. I'll never forget Dick, but he was working down the hall on mycobacterium, and he came around one day and he said, "You've inoculated mice in the brain haven't you?" I said, "Yeah." "Show me how to do it." Well I did not know whether or not it was the start of it or not, but when Eklund – Eklund visited me several times in Britain. He stayed with me at – stayed with us at the manor house. The walls were damp up that high. And I'd take him up to these – and we'd go up to see all these goats. They'd come up and chew on you and see all of these – he was excited about scrapie and at that time he was shutting down his work on western equine encephalomyelitis virus. So he was actually looking for something to do and he said when I was talking about this and working on goats that the goat was much more useful because it had a 100% take over the 35% take and you can use to assay for the agent. You've got to get it into a mouse. Well I didn't have the time or I didn't have the permit to do it. I don't know how Dick got onto it, anyway, fortunately Dick did it and that opened the whole field up.

Interviewer: And was that after you had already left the institute or no?

Interviewer: He was working on it?

WH: I wasn't aware of it. Iain Pattison had him going and somewhere in the literature, I just can't recall where it was, it may have been some veterinary journal, Pattison recounts the story of talking with Dick Chandler, walking along somewhere, and he brings up the matter of inoculating mice. I forgot what happened.

Interviewer: Yeah I think I have actually read that.

WH: Have you?

Interviewer: I have. I think Pattison was a fabulous – I mean I really enjoyed the piece that you sent to me, but Pattison was another one who wrote really nice reviews.

WH: He was a good writer –

Interviewer: Sort of thoughtful pieces –

WH: He wrote a lot –

Interviewer: He was great.

WH: He was criticized for some of his stands he took. He got off on the Cooper Zone stuff and –

Interviewer: Explain that to me the Cooper Zone?

WH: I don't know.

Interviewer: What was going on with that?

WH: We never looked at any of the sections I don't think. But he was producing spongiform changes.

Interviewer: But what was his goal with that? Was it just to show that there was another system?

WH: That I'm not sure –

Interviewer: – in which he could produce –

WH: I'd have to look back on that, what Iain was up to.

Interviewer: Because they showed that it wasn't transmissible in the way that – I mean remember they did that experiment. It's not like they were trying to say that this was producing transmissible disease, but I think they were just kind of interested in the fact that it produced a similar pathology.

WH: Yeah I forget the connection, what his rationale was in publishing all that. It's just vague right now.

Interviewer: Yeah, because it was so long ago and –

WH: I wasn't in on that, but he was doing this – see he was up in his own shop working on that, and he had a staff up there in the lab where they were doing that. One of the fellows that, who was working with him at the time, was a great fellow because he was my photographer was Geoff Millson [G. C. Millson].

Interviewer: I've heard of him, yup.

WH: And he went on to work with Hunter. At the time Geoff was working with Iain and these goats outside of the buildings and it was all in an enclosed area, with a big a fence and all that to get some movies, and he was the movie man for it –

Interviewer: Okay, so then Millson would do the photography work? He would actually do early videos

WH: He wasn't the photographer in the lab. Mr. Summerfield [spelled phonetically] was.

Interviewer: Oh okay, okay. But you were interested in capturing some of the clinical course –

WH: Yeah, I think I gave that gig to – the original footage to Stan Prusiner. Never been used, but people could cut out parts of that if you wanted to illustrate the clinical aspects of scrapie – very good. And then took it out of –

Interviewer: And why did you take those films? Was it because you knew that you wanted to work on scrapie back in the US or –

WH: No, just thought it would be interesting at the time.

Interviewer: Just interested.

WH: Well anyway, I spent three years there and my wife and I went for two years – had to give the years to pay your way over, come back and we stayed an extra year and then I could have stayed another year, but in those bucolic surroundings of rural Berkshire, my wife became pregnant.

Interviewer: Mmm-hmm.

WH: We waited until the last minute and they wouldn't take us on an airplane, we came back on a ship [First Class on the SS United States, going over and coming back, courtesy of the US government]. There were a number of job offers at the time. I knew I had to come back as something, I wanted to work on something called Aleutian disease – that's interesting working on the mink. Little did I know that was going to happen in the future. But the USDA then said, "Stay with us." And that –my transfer was simple because I was Civil Service. One day I was public health service, the next day I was USDA. So they said, well they wanted me to go to the Ames laboratory, which opened in 1961, but I said I really wasn't interested in committing myself to that place; "Well, we'll send you to Denver." They had an arthropod lab – I think they were studying [unintelligible] there. Ostensibly they wanted me to finish a meat inspection atlas, and in those days you had a lot of good pathology coming out of the meat inspection service for laboratories.

Interviewer: That sounds like a lot of work.

WH: Yeah, and the cows started dying; I said, "Well I think I could finish it." Well, anyway, to make a long story short it didn't work out that way. So I called back here, I had to find a place to live or I had to get a job, and C.B. Philip was acting director at the time because I just left Carl Larson in Paris a few months before we left – we were over there and had a nice time with he and his wife. C.B. said, "Well yeah, there's a job here. It'll take a few weeks to get the paperwork done." I said, "Well, as long as there's a job." We were in Denver at the time where I was supposed to be, and that didn't work out, so we drove here and came back to the lab and Clarence Robinson [?] was still there, the desk jar was full of the same junk as when I left it after three years. So that's how I got back.

Interviewer: Wait, before we go too far into that – I do want to go into that but back in England, can you tell me a little bit about what the relationship was like between Moredun and Compton?

WH: Oh, yes. Well they were actually rivals. John Stamp was the director at the Moredun Institute. And –

Interviewer: And Gordon had come from Moredun, right?

WH: Yes, Gordon and Pattison were both at the Moredun Institute, and that's where Gordon had his little study on the transmissibility of scrapie, with that lipodine vaccine fiasco –

Interviewer: Right, that happened up at Moredun.

WH: Yeah, that was at Moredun. And Pattison was there at the time, but just before the war – or early in the war, they both came to Compton, as I say, Bill Gordon, he was a tough Scotsman, a good administrator. He knew when some tractor driver got out of line, running his 2,500 acre estate. He lived like a Scottish [unintelligible]. But anyway, that was all part of the experience. There was this great rivalry and the orders I had when I was in the UK, anyplace I was in the UK I was on official duty. And of course I could have really use that to great extent, which I didn't. But anyway, they used to bring me up to Edinburgh a lot, I'd take the overnight train, crawl on that cold sleeper and go up to Edinburgh. So I spent a little time up there and it was usually with Israel Zlotnik.

Interviewer: Okay, what was he like? He sounds fascinating.

WH: Oh yeah, he was great. He was a Jewish fellow from Poland, I think, that was displaced during the war and wound up in Edinburgh – I think that's where he actually got his veterinary degree. But John Stamp was fine, but they always played it pretty close to the belt up there.

Interviewer: Because they didn't want to give away –

WH: Everything you're doing down there was suspect and we're not telling you a heck of a lot here. There was that rivalry, because that's the way it was at the time. Things were so uncertain that anything new that pointed to a given way, well if they didn't agree with it, it was suspect. They felt that more than W.S. Gordon and Pattison did. Pattison wouldn't – if he felt that way he never voiced it; he was too much of a gentleman.

But up there, I was trying to think of Dutherston – Dutherston was, I think, the assistant director. He was – I never got to know him too well. But old Israel Zlotnik, he never called me anything Hadlow, which was fine – Hadlow. So I'd help him take brains out – Hadlow. And we got along fine.

Interviewer: Was he a pathologist? Was that his primary –

WH: Yes, he was a pathologist.

Interviewer: Was one of the reasons you would go up there to visit was in order to work with another pathologist or –

WH: I could talk pathology with – oh, John Stamp had a background in pathology too, but Israel Zlotnik was doing all the scrapie pathology. It was great, I always liked Zlotnik. Last time I saw him I waited up for him on the high street in Edinburgh and it was a cold winter night, and he picked me up and took me to his home and I met his wife and daughter and we had a nice little dinner – nice couple.

So I used to go up there quite often but there was this rivalry and they were doing a lot of work up there trying to demonstrate the natural transmission of scrapie, and they were also interested in something about the distribution of the scrapie agent. But they were doing the same sort of animal work that was being done at Compton except I don't think their isolation facilities were as nice as those at Compton. I never really got into much of their animal quarters but it was mostly outside.

Interviewer: And when you say not as nice you mean like the animals weren't kept up as well…?

WH: Well it wasn't – yeah. They – and in terms of the isolation I don't think they could achieve – because in Compton you had individual buildings that you had to go through – not really a close [unintelligible] –

Interviewer: Washing of the boots –

WH: Boots and wash your hands.

Interviewer: So in order – so what you're saying is that at Compton they kept the scrapie away from the scrapie – they had like a scrapie-free and a scrapie-infected -

WH: Oh yes, they had a lot of units for scrapie, but –

Interviewer: But they kept everything separate?

WH: Oh they were separate, yeah.

Interviewer: Whereas at Moredun everything was –

WH: Well, I don't know how tight the isolation was, I just remember what the facilities looked like.

Interviewer: They were a bit older…?

WH: Well that may have been. Yeah, probably older because that was a fairly new unit at Compton but when I saw it in '86 it was kind of run down. I think they probably disposed of the whole thing there. But they had a great guy that used to run it – what was his name – hmm. Well, anyway. But I used to get up there quite often and had good rapport with them, in fact John Stamp and Bill Gordon came over here in November of 1950…'59 I think it was, yeah. We went on that tour, that's when I met Gajdusek in Washington. We had a good time.

Interviewer: What was it like when you first met Gajdusek?

WH: Well, we were on this tour across the States talking to sheep men because this USDA eradication program, which had been put in place about 1952, I guess, was quite unpopular, at that time they took the whole flock and killed them –

Interviewer: Without compensation?

WH: Oh yeah, there was compensation but it probably wasn't enough. Anyway, they'd kill the whole flock. And then of course Perry got in there to stir things up.

Interviewer: Did Perry come to the US?

WH: Oh yes, he was here a number of times.

Interviewer: So they were farmers or whatnot who supported –

WH: Perry.

Interviewer: Perry's theory, so that in other words they wanted to show it wasn't infectious so they wouldn't have to –

WH: That's right. That's the essence of it. Well, I saw this crew-cut black-haired young guy standing in the back while I was giving my talk and the other talks and when we'd finished he came up and introduced himself, and that was my first contact – physical contact with old Carleton.

Interviewer: Did you know who he was at that point?

WH: Yeah I probably did because I'd saw some of the pictures from Papua New Guinea, I knew this crew had this guy –

Interviewer: So you'd seen some of the pictures, had you already made that connection, that scrapie –

WH: Yeah that was published in September of '59.[Letter to *Lancet*]

Interviewer: Okay. So wait, tell me about how you did that, did you write a letter to Gajdusek also?

WH: Yeah, well it all started – it's in one of Prusiner's books, that pink and green book –

Interviewer: Okay, the pink and green book, the transmissible sponge – is that from the meeting?

WH: No, this was called Prion Diseases; I think I have a copy. But anyway, this was in June – sometime in June of 1959. Bill Jellison I mentioned, parasitologist, he'd been wandering around in Eastern Europe doing something, I think he'd been in Yugoslavia, and he stopped by – they all used to come out there and you had to take a train out there from Reading – well, out to Reading and then from Reading to Compton they had a little chauffer that used to come. And so he stayed with us I guess, but they did have a hotel – did you stay at the Swan?

Interviewer: No, I was staying in London actually, I just came for a couple of days.

WH: Oh, yeah, the Swan and go up to the Red Feather which was the pub – anyway, so Bill came and when we had dinner he said "You'd be interested in this exhibit," [at the Wellcome Institute in London] and then that whole story. So I took the train in there and saw the exhibit and put together this letter, sent it off to *Lancet*, and I sent Carleton a letter because there was a threatened printer strike in London, I thought its publication might be delayed. But he was down in New Guinea and Marianne Pins [spelled phonetically], I think, was his great secretary. She wrote to me and said that she'd send it out to him. And then he sent me a letter – I don't know whether I have it or not, I think he reprinted it in this – in Prusiner's book acknowledging it and that was the extent of it. But didn't have any contact with him.

Interviewer: But then so you finally met him, let's move up to that date again, so this was 1959 –

WH: November 1959, Washington, DC –

Interviewer: November 1959, and you had just given a talk – at a conference?

WH: No, we were talking – well –

Interviewer: It was part of this tour.

WH: It was part of this tour and it was before it. Bill Gordon would talk, John Stamp would talk and Jim Hourrigan [spelled phonetically], who was the USDA man who was running this eradication program, he would talk and I would talk and the other man, who was the head of this entourage was Sheehan [spelled phonetically] who was director of Palm Island [?].

Interviewer: Mmm, wow.

WH: Sheehan, great Irishman. That was – he was good for this sort of entourage, had a great time. So after all of us had spoken and then he came up, I don't know where I was – I may have been last, I don't know. And that's when I met Carleton. And then nothing happened after that, so that was – and then I think it wasn't until just before we left in '61 I come back, I'd gotten a telegram and some other things – wanting me to come to Bethesda to work with him on [unintelligible] and chimps. And I told him I was committed at the time, I was staying at USDA, and that was the end of it. And then it wasn't until sometime during the summer of '61, Joe Smadel was – I don't know whether he was director – he wasn't director of NIH at the time but he was –

Interviewer: He was someone pretty high up, I know, I know what you're talking about. I can't remember exactly –

WH: Tough as nails but we always got along fine. He – when Carleton invited me back there to consider taking the job, I went back and I was to work with Carleton in inoculating the chimps with [unintelligible] material. I told him I wasn't interested because by that time Carl Eklund and I had decided that we were going to work on scrapie here. In fact, I don't know whether I'd gotten the material by then. I was trying to think – I went to a WHO meeting in Rome, it was on something else, I was working on muscle disease at the time in animals and I gave some paper there. On the way back I stopped at Compton, stayed with Iain Pattison in Newbury, and asked him if I could get a few pieces of Dick Chandler's mouse brain. I got two of them, from two different passages, and brought them back.

Interviewer: What did you bring them back in?

WH: A thermos.

Interviewer: A thermos? With dry ice or…?

WH: Well there's more to it than that but I won't disclose that – there's more to it than that. In fact, we called it UK Agent A and UK Agent B, so nobody knew what we had. But that's the start of the scrapie. So Carleton said we've got to do something with that, and of course it was all – by that time, we knew the mouse would work so we'd put it in the mice and that's the whole start of it. So I think the official date that I usually use for work on the TSEs here in Rocky Mountain Lab is April 15th, 1961.

Interviewer: Okay, and you started out with mice?

WH: Yes.

Interviewer: With a mouse colony, and did you keep them separate? Like did you keep the scrapie mice separate from the other – did you create separate facilities, how did you design it?

WH: We used – I think we used Eklund's facilities at the time, where he –

Interviewer: The facilities he used to use for the equine?

WH: Western… And then I said, "Well we've got to knock it" – so this was the starter for all of it. I was, of course, looking for something to do when I came back. There wasn't any real objection from the part of the administration, I think Dorland Davis was the head of our institute at the time, and we had that sort of autonomy out here at the time and Stoenner was director – then appointed director when Carl Larson left, that would have been about '61. So Carl said, "Well, we've got to inoculate goats." "Well, where are we going to put the goats?" They had a couple of framed buildings out there, one was the old mouse house before they got the new one. And we – I don't know whether there was one – yeah, we partitioned off part of that and I made two pens in there for goats. And then I think they put a lean-to on the end of it where I could use that as the entrance, could change clothes and all the refuse would come out that way. Anyway, this all had to be approved by the USDA – as I say, it was tight in those days.

Interviewer: So it was tight, so they had been eradicating. I mean they had had this eradication program, which you had partly gone on this tour to promote, right – like this was the idea of the USDA with some of the scientists to talk about it, talk about why it's important to do this program right, to defend it in a way? And then they still – even though it was already endemic in the country – or were they not, they weren't admitting it was endemic in the country? They still – they were concerned about you having scrapie –

WH: Oh yes, because it still came under the "exotic disease".

Interviewer: So they continued to classify it –

WH: "Foreign animal disease".

Interviewer: They continued to classify it as a foreign animal disease.

WH: Oh yeah, the same way they would with Foot and Mouth when it came in, if they could get rid of that quicker, hopefully, but rather had scrapie but they were – it hadn't become widespread and it was largely limited to one breed, as it still is, a Suffolk breed. So it isn't something that's rampant in this country really.

Interviewer: So they were concerned about you starting this goat?

WH: Yeah because you had to go by the regulation with certain facilities that would meet the standard. So they sent an inspector out, he looks at it and I said, "Tell them how we were going to operate it," – I think I had four goats in each pen, all the feed came and all the manure came out –

Interviewer: Was the refuse then separated and treated differently from the other refuse for other animals?

WH: No, it was all sacked. And went right across – at that time it was just across the road to the incinerator that they were using at that time, it was all – yeah. So that – the inspector said, "Well what do you think?" I said, "Well it sure as hell has gotta work, I'm not working on Foot and Mouth disease virus; it's going to be adequate for scrapie." So I got the permit to do it. So we inoculated goats and when I came down fine, that was with the stuff I brought back, Chandler's stuff.

Interviewer: So they continue – you continued to get the same sort of 100% rate that Pattison –

WH: Oh yeah, I think I got 8 out of 8. And I got some good material to study. And then, wanted to do a pathogenesis study, but you needed more goats and more room.

Interviewer: So why – okay, I think this is really critical; why did you want to do the pathogenesis? What was driving you to do those studies?

WH: Well that was Eklund's view of any of these infectious diseases, what is the distribution of the agent, the virus? What is the pattern? What organs are affected? Where does – what are the favored sites of replication, and things like that? And this of course is what we [unintelligible].

Interviewer: So this was Eklund's philosophy about how to go about figuring out –

WH: Studying infectious disease. He was of the old school and that was emphasized. So my background in infectious disease was so-so, but I learned a lot from him. So anyway, we had to get more goats and a place to put them and we didn't have the facilities to handle that many goats. So there was a cattail patch back where Armco – I still call it Armco sits –

Interviewer: What's that stand for, Armco?

WH: Armco, that was the name of the manufacturer. [American Rolling Mill Company (1899-1948; Armco Steel Corporation (1948-1978]

Interviewer: Oh okay.

WH: And it was self-framing steel buildings. I think it was the first one here in Hamilton because they came out here and took pictures of it for their advertising.

Interviewer: Wow.

WH: Being used as an isolation room for goats.

Interviewer: That's fantastic. They didn't tell them that, did they?

WH: I don't know. But anyway, I remember them coming and taking pictures of it. So, well we had to get money and I shouldn't go into that because that'll get me into hot water, but we got money.

Interviewer: You're not going to – how can you possibly get into hot water anymore?

WH: Well, we got money. There was a local group at the time that were really supporting the lab – businessmen uptown. There's a banker, a fellow who owned a car dealership, editor of the weekly paper in this end and maybe someone else. Carl Eklund and I went downtown and met with them in the old bank building. [Ravalli County Bank original 1895 building located on Main Street in Hamilton, Montana] I told them what we were up to and we needed $20,000. Well, we got the $20,000.

Interviewer: Okay.

WH: We got the $20,000 so then – and in those days we had the $20,000 to work with here, it didn't have to go through all of the... So I remember going to Missoula to the Wright Lumber Company where they had an Armco representative and I designed the building – knew what I wanted.

Interviewer: So you were there –

WH: I did all the designing. Yeah, yeah.

Interviewer: Wow.

WH: Sheds too, I designed the whole works, I had to; there wasn't anybody else to do it. Well, we had it built and they had a good technician to do it – they had a mechanic that came out –

Interviewer: And what would be important features that you wanted to make sure were included in the design?

WH: Well, I had to have pens, I think we had…4, 5 – no 6, probably 6 pens that were roughly 10x10, and two pens that were maybe 10x15. It had a central alleyway and we made them so that the partitions could be moved; we had these big planks drop down in the channels. We had to have floor drains, and on one end we had the entryway with the toilet and shower – you can change clothes, and the other side of the alley was a feed room where the feed was delivered. Then on the end of this alleyway, you get rid of all the manure, the refuse in plastic bags.

Interviewer: And then were people required to wear special boots or to wash off their boots after going in and out?

WH: Yep, yep, everybody did. Only dealing with men in those days.

Interviewer: Of course, yeah.

WH: So that made it a little easier as far as the design. But anyway, so –

Interviewer: So everyone had to change completely? Like you're talking like –

WH: Well the way they do it –

Interviewer: Take off all their clothes and take a shower in order to make sure they were decontaminated?

WH: Yeah, well we didn't have to do that.

Interviewer: Then why would it matter if it was men only?

WH: Probably wouldn't there, the mouse unit was a little different deal. Well they had to shower out, had to shower out so – yeah they had to shower out because you had to walk through the shower, you came in, you left the clothes that you came in with and you already had deposited your street clothes somewhere else and you had the lab coveralls on. Well, you would deposit those here and go through a shower area, whether you took one or not, to where the toilet was and where the garments were that you wore into the place.

Interviewer: Oh I see, okay, yep that makes sense.

WH: Anyway, then you had to arrange for heating and that took, as I say, too much time doing that service stuff. But anyway – and it had to be fly-tight –

Interviewer: Were USDA inspectors worried –

WH: They inspected that.

Interviewer: About flies transmitting it or something?

WH: Oh yeah, yeah. And then where I decided to put it was this cattail patch, they had to fill that in. And C.B. Philip was still director, that would have – I guess he wasn't – I guess he was director then, it must have been '62. Yeah, '62. I told him where I wanted to put it, he said, "Oh God," – and I was going to use fly spray here. Well their insectary was downwind from that. "Oh, you just can't do that, you've got to put it clear back on the brow of the hill." I said, "Well I'm not going to put it way back there." Well, as he told me later he lost a few nights sleep over that.

Interviewer: They had an insectary – oh, the ticks!

WH: Yeah, they raised all their –

Interviewer: So they were worried that in spraying insecticide it –

WH: It'd suck into the – because they were downwind, it was on the north side of that animal building at the time, that wing.

Interviewer: So did anything happen when they –

WH: No, I don't think they ever used the spray.

Interviewer: Oh good.

WH: Never used the spray. I just told the USDA if I had to I would. The windows were screened – ventilating system up at the ridge was screened –

Interviewer: So you just kept them out of it, you kept the flies from getting in – yeah.

WH: Yeah. Oh I don't know, if there were a few flies that got in we dealt with those, but in general you just [unintelligible].

Anyway, that worked out fine. Then we built a second one just west of it and used that for progressive pneumonia of sheep. Then I had to have some outside facilities to hold sheep so that they were sort of quarantined before we brought them inside, and I had two pens built down west and I think those sheds are still there. Then I had to have a hay shed – had that designed and – I designed and built it. At the time they had their own mechanics here; there was a refrigerator man, there was a painter, a plumber; it was really overstaffed but it was a nicety and they had a machinist that was good – he made little jigs for me to inoculate mink that were as slick as could be]. Anyway, they had a good carpenter, Frank Taulman, he was a carpenter but he was a contractor too before he came to –

WH: He did a lot of work on these Armco buildings. I had to put wainscotting inside, the plywood, and he did that. Anyway we got it built on a shoestring, didn't have an architect. I remember meeting up in the administrative officer's office one night with the representative of the Armco Company from Mazola and I had the plans there and I said, "Now do we need an architect?" "No," he says, "I've got a draftsman that will draw them up. All we really needed them was the concrete people and the plumbers. Otherwise the Armco went up. So anyway we got that. That was – yeah. Well then I had to find goats and sheep and goats were hard to find. You had to really shop around. I got them locally and I knew enough about goats. I grew up with goats.

Interviewer: What special specifications were you –

WH: Well these were dairy goats and most of them were Alpine Nubian breeding, Nubian with the long floppy ears and Roman nose. The Alpine was a popular one and they were all dairy goats. Some Toggenburg and then some Saanens and then – so I had enough decent goats. We had them in the holding pens down there and we got a look at them and before we brought them in to inoculate them. And then because of the shortage we were going to breed our own.

Interviewer: There was a goat shortage?

WH: Yeah it was tough getting goats. So I had this great big Saanen buck, a white Saanen. We bred goats there and we good kid goats every year. Did that for quite a while. I had a good goat man, old George Wilson.

Interviewer: Was that artificial insemination?

WH: No.

Interviewer: Or was it all just…?

WH: It was all natural.

Interviewer: Natural.

WH: Yeah.

Interviewer: Wow.

WH: And of course the stinky old man goat, fortunately he was way back at the end of the property, along about September they get a little fragrant.

Interviewer: So you bred your own and did you sell any back to the community or did you use –

WH: Oh no you couldn't. In those days nothing went out.

Interviewer: Nothing went out.

WH: It went to the incinerator and –

Interviewer: So every goat you bred stayed at this facility –

WH: That's right.

Interviewer: Or was incinerated? Yeah.

WH: We had one exception in the end we got into the breeding pigmy goats. I used those when we inoculated Creutzfeldt, the output material in the goats I used those. I think the last buck I had they did send that one somewhere. He had been outside all the time. Otherwise, well, we bred goats and old George Wilson was a good goat man and I always had a good supply of young healthy goats.

Interviewer: That's great. How many goats did you have like at – when the facility was really up and running?

WH: Well there would be probably several hundred.

Interviewer: Wow, so several hundred, at any one time some of them would be in the isolation facilities, some of them would be out.

WH: Most of them would be inside I think. We had 10,000 mice all the time doing our assays and which you couldn't do anymore and –

Interviewer: So this is an incredible – I mean –

WH: About a thousand mink.

Interviewer: I think this is really important though, too, because when you're talking about the kind of work that you had to do to do the pathogenesis experiments that you did. I mean you're talking thousands, right? I mean because the goats and then especially the mice and then when you're doing the bioassays and the titrations and each titration involved what was it like six different or was it four I can't remember.

WH: Well we'd usually run it out to – it was at least – well you could get away with five, but usually 10 mice per dilution and you'd run six dilutions.

Interviewer: That's just an incredible amount of animals and I can imagine – I mean can you tell me something about like the time and the labor and the effort?

WH: I've only had one person that really recognized that and mentioned it at a public – at a meeting. That was – he did a polio. What's the other polio vaccine?

Interviewer: Sabin, is it –

WH: Oh Albert Sabin. He was an old hard nose and this was at some meeting back in Washington, and I presented some of the preliminary stuff on the pathogenesis in mice and he got up. He had just gotten through really running somebody into the ground and I was wondered what sort of response I was going to get from old Sabin, and he said to everyone, "Do you know what that's involved?" And he went through the number of mice just what you said, because he knew that kind of stuff. He was one of the old school like Eklund. Anyway you couldn't do it. Well –

Interviewer: And he could appreciate what that meant.

WH: Right off. To get those significant points on that table the amount of work you had to do, he was impressing the audience with that.

Interviewer: That's good, because I can't –

WH: And I think that's in print.

Interviewer: Really?

WH: It's in print.

Interviewer: Is it?

WH: He did like a transcript of that or something?

WH: It came out as a book and these were the question and answer things.

Interviewer: So this is from what? From a special meeting?

WH: Yeah.

Interviewer: What was it called? I mean I'm just wondering if I could look it up.

WH: Oh yeah, I have the book.

Interviewer: Okay, maybe afterwards you can show me. Yeah. Because to me I think those experiments that you and Eklund initiated, the pathogenesis experiments, I mean are still cited as some of the…because I mean there really hasn't been – I haven't seen anything that really replicates or comes close to it.

WH: No that's unfortunate I think, because we'd often wanted to have it replicated to see how far off we were and to see whether it is consistent.

Interviewer: So what was the division –

WH: To corroborate it.

Interviewer: Of labor like? Like who did what in this whole – you mentioned Wilson, was that his name, who was taking care of the goats or who was –

WH: Well they were all worked – I was running the show. Carl Eklund and I, that was our project and Carl Eklund had working with him was Dick Kennedy. He was great as a lab man and instrument man and his – and Carl's secretary was Lola Grenfell and he'd trained her and she could do all the calculations on the endpoints and –

Interviewer: So she would take the hard data and analyze it?

WH: Mmm, hmm.

Interviewer: Like produce some of the – at least the cursory –

WH: And tell you what was wrong.

Interviewer: A sort of analysis?

WH: Yeah. That's above titration and so he had that end of it and of course he was thinking all the time things to do. You couldn't keep up with him, but I had all the grunt work, all the animal work and at the start I had several veterinarians just out of school that helped me as far as the clinical work. There was a lot of clinical work to do and then just helping with necropsies. You know just cutting a sheep or a goat –

Interviewer: So explain – so with the clinical work what would they do? How often – like they'd go examine an animals –

WH: At least once a week.

Interviewer: Once a week.

WH: Yeah. Of course you've got the caretakers there too that would inform you about – some were better than others. I had to train caretakers. This is the way you handle here not the way you do out on the ranch. It was a little different and I had a good crew at the end. I had a good sort of foreman, Gilmer Reich. Before that I was having problems because between me and the animal caretaker there had to be somebody else. It was doctor that was telling them. So when I got Gilmore Wright we got the crew settled down and well trained.

Interviewer: So Gilmer Reich was one of the veterinarians?

WH: No he was an animal caretaker.

Interviewer: He was an animal caretaker. He was able to run the animal caretaking show.

WH: Yeah.

Interviewer: Because he could handle that – manage that, which allowed you to then focus more –

WH: I knew that was being –

Interviewer: On pathology –

WH: Taken care of.

Interviewer: Hmm, mmm. So you were involved in both the clinical part and the pathology part?

WH: Yeah the whole works.

Interviewer: I mean obviously –

WH: Everything having to do with the animals, because I had to set up the whole system of husbandry, find sources of feed. We had difficulty getting good hay. I remember turning down about four loads of hay in a row.

Interviewer: Why what was wrong with it?

WH: It was moldy and a fellow called me that was supplying it and he was upset. "Where are you from?" I said, "I'm from Ohio." "Well this is what hay is like out here." And I said, "You don't have to tell me what alfalfa hay is like. I know good from bad." And so we had a little tussle there for a while, verbal tussle, and that was the end of that. Anyway I found some good hay down in Idaho and I had a fellow haul it in and he'd stack it, because I was just feeding them good alfalfa hay and it would keep these goats – I kept them inside for what 8 years or more and I don't think they were – their well being was looked after. Maybe they didn't socialize the way some would want them today, but they were well feed and as long you keep sheep and goats' feet trimmed you're not going to have any problems. That was one part of the ritual. I had to establish all that. Well and then I had a few young veterinarians that would come and at least assist me with some of the clinical work and well some of them were all right. The best one, of course, was Rick Race. He joined me in 1972.

Interviewer: And where did he come from?

WH: He was right out of Colorado, right out of school, just got his veterinary degree. And the reason we got him is because he had experience with mink since he was in high school and I'd been working with mink for about 10 years and I needed someone that understood mink. I was learning, and I learned a lot, but I needed someone who was familiar with mink, who could handle them.

Interviewer: Because mink are difficult to handle?

WH: Oh yeah, yeah.

Interviewer: What do they do? Just because they are rambunctious or…?

WH: Oh you have to wear heavy gloves or they'd grab everyone. You have to grab them a certain way or they're going to nab you. We had a good animal caretaker that dealt with the mink. He was good Bill Anderson. He'd call me every morning and tell me something about this mink or that mink. You see he knew them individually although we had a lot.

Interviewer: That is great, that's incredible.

WH: And so and then Rick would be out there and Rick helped me with a lot of the post mortems. I must have gone through 3,000 mink taking brain, spinal cord, the works, out of 3,000 mink in the time I was working on it and Rick helped me with some of that necropsy work to, but he was good and he did all the mouse work; supervising inoculation, running the assays, and collected the brains that we needed because I used to do histology on quite a few of them.

Interviewer: Did you train him how to do histology also?

WH: No he just collected –

Interviewer: So he was more – he stayed more on the veterinarian end in terms of he would do the post mortems and supervise the inoculations, but he didn't do the microscope work?

WH: Well he looked at a few, but he didn't really get into the science until he joined Bruce Chesebro, got into his work, which was fine. So anyway Rick was great at that and we had quite a show going until it collapsed.

Interviewer: Okay lets not go to that yet. TME, mink encephalopathy, how did you get involved in that?

WH: Well I was – this was in spring of 19 – no it would have been a later than that. Maybe July /August of 1963 the director came to me and he said he got a call from CDC somebody had gotten in touch with them, they think they have toxoplasmosis in their mink in Blackfoot, Idaho, would you check into it. So I got a hold of the fellow named Jones – I called him or wrote to him I said, "We're interested in this toxoplasmosis, I can tell, but I have to have a couple of sick mink or dead mink." So we had – my wife's sister and her husband were visiting. It was on a Saturday. Here comes Jones dragging in two mink. So anyway they were showing good clinical signs. Did necropsies and I had been working –

Interviewer: What kind of clinical signs were they showing? Like were you surprised by the signs or did it look like it could toxoplasmosis or –

WH: Well I didn't know about toxoplasmosis in mink, but there was ataxia, hyper-excitability, some had tremor. Anyway took the brain and cords out and I'd been working with – I had a strain of toxoplasma here that I'd gotten from Ohio, I'm not sure what I was up to at that time, and you could keep it going in mice. So I inoculated some mice with material from these mink. Well they didn't come down and then in a very short time. Meanwhile I'd sectioned the brain and saw the scrapie like lesions. So told Eklund and he got excited. So we went down to see old Jones at Blackfoot. He didn't have many mink left. We collected a few more and then Eklund said, "Of course we've got to demonstrate that it's transmissible." Well I had a few mink because we were just beginning to get some mink to work Aleutian disease. I didn't have any decent sheds, but there was a little building we called the horse barn, which is long gone, where I hung a few – I'd already built cages. I knew how to build cages for them. Hung them in there and I had I don't know half a dozen mink I guess that we inoculated just –

Interviewer: Would they hang the cages?

WH: Well you hang them on nails. They're about a cube. The design I used you couldn't use them now I guess, but they worked for me. I got a lot of help from a mink rancher up at Conner [Montana] as far as mink husbandry and things like that. So we inoculated some mink and just intra-peritoneally, I think with brain material, and then I was talking with John Gorham over at Pullman, it was about that time when we were in Pullman, Washington, he was a friend of a colleague that I'd been in touch with for years. He was a mink veterinarian and I told him about this disease that I saw down in Blackfoot and he said, "Oh yeah, I heard about that and we were going to send so and so down to look at it." I said, "Well it's too late I've already looked at and this is what it is." He said, "Well I've also heard of disease that sounded like it might be similar in Northern Wisconsin." And the big mink veterinarian in Wisconsin was G.R. Hartsough. So John said, "Get a hold of Hartsough." So I called Hartsough. "Could we go up and look at them did he know about what was going on up there at Hayward." He said, "I'll meet you at Saint Paul." So I flew to Saint Paul and we got into his car and drove up to Hayward and stayed up there. It was little fishing area in Northern Wisconsin. The next day we went out to the ranch. There were about 100 mink left of the thousands they had and all of them were sick.

Interviewer: So this was practically simultaneous –

WH: Mmm, hmm.

Interviewer: To what you were seeing in Blackfoot?

WH: Mmm, hmm.

Interviewer: This was happening in Blackfoot the same time it was happening in Hayward?

WH: Mmm, hmm.

Interviewer: And he was dealing with it there and when you say he was a mink veterinarian like was he someone who sort of was called in by mink ranchers often to treat their –

WH: Yeah he was a consultant. He was the whole mink industry and yeah he was the one – I don't think John comes quite that close, but old Hartsough, he knew the whole mink industry as well as diseases and they all looked to Hartsough. Well we had gone up there and I think I did close to 10 or 12 mink the sick ones. Did it out on a picnic table and didn't have – in those days I was collecting stuff that I could freeze and they didn't have the Nunc vials that you could screw the cap on. You had to fuse them shut that was used. I said, "What do you got here, I didn't bring anything?" "Well we got a handy man or a mink man around there." Well, his welding torch. We got that set up. So we sealed all of these ampules and then went up to a fishing area so I could get dry ice. So I got dry ice and packed it all in dry ice and in those days I got away with bringing it home on the plane.

We brought all that stuff back and I never used it. That sectioned of the brains, of course, was the same stuff and then I think – well I don't know what happened but I think probably what – I don't know whether they had ever sectioned the brains at Wisconsin and recognized the lesion as that of scrapie, but Dieter Burger and Hartsough – I told Hartsough why I was interested. I said, "The damn thing looks like scrapie." Of course he was [unintelligible] with the people at Madison.

Interviewer: Burger and those guys.

WH: That's how it worked. Dick Marsh knows the story, which he has published, and he credits me, but that doesn't make any difference.

Interviewer: He credits you with knowing the similarity to scrapie.

WH: Yeah.

Interviewer: And that I haven't seen. I will have to look for that, but that's great.

WH: I can give you the reference.

Interviewer: Yeah. And so that it was then it was following your lead perhaps that they started investigating it as a –

WH: Well, all I had to tell them was that it looked like scrapie and Burger, the virologist, yelled out, "We're going to inoculate animal!."

Interviewer: But you had already inoculated some here?

WH: Yeah.

Interviewer: Right? Yeah.

WH: And that's the story, too. Well anyway we did that. So I inoculated these animals and then I think it was September so that would be September, November, December, January, February, March, April, May – yeah, about 8 months some of them were getting sick. Showing signs of TME.

Interviewer: That's pretty quick.

WH: And I was, "Oh, that's transmissible." We inoculated mice and they didn't come down. So the conclusion is, "Ah ha! It's different from the scrapie agent." Well there's a story to that too later, but then I had accepted an offer to go to the Soviet Union with five M.D.s to look into the matter of whether they actually had demonstrated the transmissibility of Lou Gehrig's disease, ALS. And the darn mink were coming down out there. I said, "Carl I can't go." He said, "Go ahead. We'll take care of it." So he and I, forget what veterinarian was here at the time,[Colden C. Boyle preceded Jackson and Whitford] Some of them were here for just maybe a year or so. So anyway they collected the material and Carl made clinical notes for me so when I came back – I was away for 6 weeks I guess. I was around Siberia.

Interviewer: That's a long time.

WH: Anyway –

Interviewer: They collected the material while you were gone.

WH: Yeah. So anyway we demonstrated that it was transmissible. So that's the story. Before that Hartsough was the one that first described it in 1947, and at the time they had submitted some of the brains to a pathologist. I won't mention who it was, and they concluded it was probably a neural toxicosis. They saw the spongiform change – a degenerative change. It wasn't an encephalitis and then that's it and then when it recurred in the early '60s about several farms using the same feed. It was quite obvious that it was coming from the feed, but then one had occurred again in '63 in Wisconsin and Idaho and we demonstrated that it was transmissible and that brought it into the TSE group. It was actually the second animal and that was before Kuru was demonstrated transmissible.

Interviewer: That's true – that's amazing. You're right, so it was the second – really it was the second one that was demonstrated.

WH: That was actually demonstrated, yeah because Kuru they didn't report that until '66, seven years after the similarity was brought to their attention and that was the second one.

Interviewer: And was the thought at the time about the relationship between scrapie and –

WH: Scrapie and – well we at the time the thought was well it looks enough like scrapie that maybe that's how they're becoming infected. Mink ranchers feed hellish gamish of stuff, but old Jones down at Blackfoot and we didn't pursue that and I never got the whole story there either. He was concerned because he was feeding skinned beaver carcasses from Utah. He had a whole locker full of frozen beaver carcasses. I brought some back. I' m not sure what we did with them, but we didn't pursue that. Then up in Wisconsin again your initial reaction was, well, the mink ranchers including some scrapie infected sheep. Well, as the way it turned out even if you look back at those early days most of these ranchers say they didn't feed sheep, but cattle, these downer cows, and certainly in the last outbreak in '85 at Stetsonville [Wisconsin], Dick Marsh is quite certain that this rancher fed nothing but downer cows for 30 years.

So that gave rise to his conclusion that there is an encephalopathic agent circulating in the cattle population in this country and he got into some things. Dick would get quite steamed up. Yeah, I really miss Dick. He would get quite steamed, but I think what he failed to --and this whole thing got mixed in with the mad cow stuff and that whole story. I think what he failed to recognize is that there probably is another spongiform-causing agent in cattle, but it might not produce the same picture as BSE clinically or under the microscope. I think he just didn't see that, but it was – and I think everybody is missing it now. I put together a paper and I can give you copy of it –

Interviewer: I would love that.

WH: It is some comments on that to sort of counter the baloney that I've been hearing locally, but I think you have – so I agree so it came from cattle, but we still haven't explained how it all came about. And if there is such an agent in cattle it doesn't surface very often in fellows that are feeding downer cows, and it isn't the cause of most downer cows, because Dick then showed that this agent from Stetsonville would produce neurologic disease in calves. He didn't pursue that enough, for one reason or another, but then in the end we put his material which would have been second passaged back into cattle and they came down nicely. We took the Hayward material that had been in the deep freeze for 28 years and that produced the same disease and the stuff I had from –

Interviewer: In the cattle?

WH: Yeah.

Interviewer: The same thing? Yeah.

WH: So –

Interviewer: So you did the Blackfoot, the Hayward, and the Stetsonville and they all produced the same clinical symptoms and pathology in cattle?

WH: Hmm, mmm but I did the pathology. I wasn't over there to see as much of the clinical sides that I would have liked because I don't think people recording it didn't record it as in detail as it should be. A few times I was over there, I said, "Well what do you see?" "Well, but you missed this, missed this, you missed, you missed."

Interviewer: So they were missing some of the subtle signs –

WH: Yeah the subtle signs –

Interviewer: That cattle were...

WH: So there may be a pathogen out there –

Interviewer: Did you say they had an ear thing? What were they doing with their ears?

WH: They're doing this.

Interviewer: They'd move their ears, wiggle their ears kind of…?

WH: Mmm, hmm. And you just have to have some feeling for the animal.

Interviewer: What a normal would like and –

Interviewer: Hmm, mmm. How a given animal –

Interviewer: Peculiar.

WH: A sheep behaves or how a cattle behaves under certain circumstance. You just – I always tell people you don't have to have do a neurologic exam on an animal to diagnosis scrapie. You just stand back and watch it, get it to perform a little bit. When I was in – the summer I spent in England with Gerald Wells they only had about 8 or so infected cows there all the time. I used to go down every morning and just watch them perform.

Interviewer: So was this during the – was this when they were doing the experiment at VLA where they were infecting – where they were kind of doing their cattle pathogenesis? Is this what you were helping them with?

WH: I didn't – I was there. All I did was – the summer I was there. I was helping Gerald [Wells] establish the topographic distribution of the lesion and the emphasis was always put on the vacuolation, which included vacuolated neurons as well as the spongiform changes the way they used the term, and he assigned me diencephalon. Well we had a – Matt was from – excuse me – from France. They would identify all of the thalamic nuclei. I said, "We don't have to look at every damn nucleus." "Yeah well…" So I did that for 100 brains especially in the meanwhile I looked at the whole brain, and the beautiful sections, you'll never find those anywhere. He claimed they –

Interviewer: Who took the sections?

WH: Cost 150 pounds to do one brain like that. And his wife was working in the histolab at the time, sections like that.

Interviewer: Just gorgeous like large…yeah.

WH: Just no artifacts and beautiful. So it was a real treat to study that. Well that was what I was doing, establishing the, I call it, the topographic distribution. They like it to call it the profile. It's a profile and he still hasn't published that in its entirety.

Interviewer: You're kidding?

WH: He still talks about it. He published some of it.

Interviewer: Right I have seen some papers.

WH: One of Prusiner's books there, but well that's – a few things on the pathology of BSE that should be…

Interviewer: To thoroughly study.

WH: Yeah, well with special stains.

Interviewer: The astrocytic response.

WH: Admittedly when I was looking at all these sections I was never impressed with any astrocyte such as you could appreciate in animal with scrapie or a mink with TME. It was just a H&E section, because all you're doing is looking at the naked nuclei. But I thought, especially the cerebellum, because in my experience with the routine stains of the cerebellum, the cerebellum cortex, I was never certain that I could really appreciate the extent of the astrocytic response until I put on something special, and I have had no experience with the technique that is used now the GFAP. I have no experience with it, but the material that I have looked at doesn't come up to a good old [unintelligible]. Of course you couldn't do it now just because we were using mercury, but we had a technique that I'd gotten from old Peter Dennis, my histo man in England. They were well trained. They did a lot of on the job training and he was well trained. He'd gotten his training at the Radcliff Infirmary in Oxford and I had the technique and there were just a few tricks I think that make it work that you don't get out of the recipe books.

Interviewer: Like what types of –

WH: Well use brown-gold chloride not yellow. I don't know why. There is a different valence on the gold, but the brown-gold chloride, I could get it from Germany. I still have some down in the refrigerator.

Interviewer: Wow.

WH: Then a few other little tricks.

Interviewer: Like what? I mean like what kind of…?

WH: What did we do now? We put something in the water bath to take the wrinkles out – no that wasn't it, because we had to dehydrate them on the slide. In England we did it under toilet paper and the toilet paper they had in England at the time was real good stuff. It was pretty heavy stuff. It didn't come ready rubbed as they used to call it. Anyway but so you didn't do it the usual way. You dehydrated them under this paper and there was a way of – I've got it in the notes down there. There were few little wrinkles like that but I think the main thing was using brown-gold chloride to make up the sublimate.

Interviewer: And that would help you – this was to get a good stain of the astrocytes?

WH: Oh yeah. Did you ever see one of those? They're just black.

Interviewer: I have, I've seen pictures, yes.

WH: Beautiful. And the other thing of course is to fix it, the tissue fresh preferably in formalin ammonium bromide for a few days.

Interviewer: And what does that do?

WH: It acts as a [unitelligible] for this impregnating technique that you use with the gold chloride.

Interviewer: So that was a critical…?

WH: Yeah, yeah. You could do it on formalin –

Interviewer: Combination .

WH: Fix but you never got as nice – as beautiful – beautiful sections would come out of that. All the mouse stuff – what people forget is that – well a couple of things. We worked with a wild agent right out [unintelligible], and they behaved differently. If you've worked with these lab mouse stuff it is all predictable. They're going to come down on a given period in a group and they'll look alike, but with the wild stuff that isn't so. It is more ragged, clinically a little different, and you can't use the incubation period as the end point, which they do now. It is all right if you've got on a given tissue, in other words if you get brain, which you passed or you could use the endpoint – the incubation period endpoint to derive the titer, but [unintelligible] Eklund he used the old – you had to run it out. So, anyway, there were always some questionable. The obvious ones clinically, well that's scrapie. We had our own little way of identifying them, because we looked at them and Rick looked at them every week and the caretakers looked at them every day, but I would look at least some from each batch microscopically and I didn't worry about Dickinson and –

Interviewer: The lesion profiling?

WH: Yeah, the lesion profile looking for holes.

Interviewer: Why? Why were you –

WH: It wasn't necessary, an astrocytic response comes up right away in the spinal cord. You could confirm a diagnosis of scrapie in the mouse by one section through the spinal cord with Gal stain on it, because the astrocytes in the gray matter just light up like that.

Interviewer: And there is no other disease that looks like that?

WH: No, not that I know of and as far as the mouse ages and getting out on the titrations that go 18 months to reach an endpoint, you'll see a few but you get used to that, that age mouse. We used to have a little game. Obviously it starts in the cord, that does in the sheep and I had a difference with Richard Kimberlin about that. They talk about pathogenesis of scrapie. Then he drags out what he observed in a mouse. That doesn't apply to a sheep. This is one of them – but in the mouse you could –

Interviewer: So in the experimental model – so here this is a case where you feel that there's a difference between the experimental model system and the wild type disease and that it can sometimes be deceiving.

WH: It is – well it is misleading and I think this maybe harsh – too harsh a way of saying it, but I think so many of the observations on these models they offer interesting biologic phenomenon, like the recent one of finding the agent in the skeletal muscle, but I always pass them off – a lot of them off as laboratory artifacts and they are misleading. Certainly, they are misleading if you're interested in information that contributes to a better understanding of what is going on in the natural disease. Admittedly there are limitations in working with large animals but – and you get clues like we did with mouse that the agent replicates in lymphocytic lymphoreticular tissue, and it so happened that's true in the sheep and it's true in deer. It is not true in BSE. It is not true in TME.

Interviewer: Right, right which is interesting. It is very strange. I mean – but what about natural disease versus experimental disease in the sheep? Let' s say you take a natural host but experimentally inoculating it with an experimental strain of scrapie versus naturally it getting infected in a heard situation.

WH: Well I'm sure there's some – I think essentially the disease is the same. There's some little difference in the lesion. I don't think – I think as Zlotnik pointed out there are probably far fewer vacuolated neurons in the experimental disease in sheep. Certainly with goats, the agent received quite a few passages in goats which achieved two things it shortened the incubation period drastically through whatever mechanism they want to ascribe this adaptation, and then produced the more severe spongiform change. The thalamus of some of these goats that I have just looks like a honeycomb. You never see that in the natural disease to that extent. The same way with the Kuru and then the chimp. But there are some difference. I think when Gerald Wells' experimental inoculation with the cattle with the BSE agent that found as far as – I think clinically it was probably essentially the same and you can't draw a very close correlation of the clinical signs with what you find. You know it is not that cut and dry. There are obviously things going on in the neurons that you – that aren't every going – but he found that lesions in the thalamus were a little more severe in the experimental disease as opposed to the natural disease because in the natural disease by the time you get up to the thalamus it sort of peters out. So it all obviously starts caudally, all a part of the medulla and you can see it go up through the pons and the midbrain around the periaqueductal gray matter, and then when it gets up to the thalamus, to the diencephalon, it will hit some of the thalamic nuclei in the midline of hypothalamic in the midline thalamic nuclei. But it doesn't knock out these big ones like scrapie does, and I'm not sure whether – I've looked. One nucleus that always gets knocked-out in the chronic wasting disease, scrapie and TME is the caudal colliculus, the auditory relay center.

Interviewer: Right. So but here – so we were talking a little but ago about astrocytes and so for you, especially when it when it came to like the quick diagnosis, a sure fire diagnosis, taking a section of the spinal cord and finding these dark black stained astrocytes using this technique was to you a definitive sign. Now what about the spongiform change? What about the vacuolation inside the neurons, the pericardium?

WH: Oh yeah didn't spend any time on that in the mice. Maybe early on I did and I can't recall what I put together, but running the bioassay the standard one was to – on the few mice that we wanted to look at, some of these mice would get obese and that would sort of mask the real clinical picture and you see that and others have described it in some of these scrapie agent isolates will produce fat mice. I've noticed it especially in the wild agent. We took a midsagittal section of brain and you've got tell these people when they take the brain out it goes clear back, you don't cut out it off right behind the cerebellum, you want the medulla; if you're just taking the brain as I've had some of them were just taking the brain out to make tissue that's all right, but not when you're going to section it and two cross sections of spinal cord and, of course, the mouse had been – the skin is bent back and you just cut those chunks through the muscle, bone, the whole works with a razor blade, put them in formalin ammonia bromide and it has a sufficiently low pH that after two days it decalcifies the spine so you can cut the whole thing – you cut it on frozen sections and then when you float it, the cord drops out and you've got to take care of that one spinal cord, because you got rid of everything else, but that works fine. And so the standard one, I might have a slide in the basement I can show you – sagittal section of the brain and two sections of spinal cord.

Interviewer: And that was it that was all you needed?

WH: Yeah and I looked at them, as I say, "Cold." Rick [?] took all the clinical notes. When they came to me it was a number. I didn't know whether it was showing signs or not and then I would make my diagnosis and then check with his clinical picture.

Interviewer: Cool, so that was the way you did, that was the way you went down the line? Now with lesion profiling my understanding is what they were trying to do was develop a system where you could differentiate strains of scrapie type agents based on the amount of vacuolation or whatever in different part of the brain. Now, but do you think it can work for that purpose?

WH: Well that's the only basis that has been used for identifying so called strains of the scrapie agent, some 20 strains that Dickinson and…I can' t think of his name. I forgot.

Interviewer: Hugh Fraser.

WH: Hugh Fraser.

Interviewer: Was the one who did a lot of that.

WH: Yeah he spent a little time with me here. Hugh Fraser and Dickinson –

Interviewer: How he did? Did he come here to RML?

WH: Huh, uh.

Interviewer: Really?

WH: He was here for maybe a month. Dick Chandler came too.

Interviewer: Oh wow.

WH: Yeah.

Interviewer: And this was after you had been there and come back.

WH: I came back here. That was sometime in the – it may have been sometime in '61, summer '61.

Interviewer: And did you help train Hugh Fraser?

WH: No.

Interviewer: Or was he already fairly well trained?

WH: I don't know how he was sponsored but he came here. He was doing some metallic impregnations while he was here and I was too busy with other things, so he was on his own. He was just here and Dick was the same thing. I can't remember what Dick was here for, but they were here. Well that's the basis for identifying so called strains.

Interviewer: But it was never something that you performed here?

WH: Oh no.

Interviewer: Yeah it wasn't something you cared about really?

WH: No it – and you know it is not as simple as you might think. They make number of passages of this various isolates and then put them in with different stocks of mice and then, depending on the incubation period and the topographic distribution of the spongiform changes, they identify or use those as identifying features of the different strains, but I've never done that didn't have need to. And I – you know it's laborious. The last I heard, because it came up with the whole BSE story, is we don't know enough about the different, if there are, different strains of the scrapie agent that are extant out there in the British sheep population. They've got, what, 40 million sheep. And so I think Gerald told me that they were looking at – well I thought he said 60, but that would be a chore, 60 isolates but anyway they are looking at more isolates to see if there are some differences.

Interviewer: Right trying to characterize them better. Yeah.

WH: So they might find one that looks like BSE I don't know.

Interviewer: Right. So then you were here – at one point did Stanley Prusiner come work with you?

WH: Oh Stan, I just have a rough – I would say it was about '72. I got call – or maybe it was letter I don't remember, I'd have to look – from this fellow Prusiner he was interested in working on scrapie and he couldn't find anybody to do his animal work. So I talked with Carl Eklund about it and Carl said, "Oh yeah you do it. I'll set it up to do it," and then we were. We had quite a set up to do mouse bioassays. And so Prusiner came sometime in ' 72. He took the bus from airport up to the edge of town and so I went out to meet him and here's this young lad out there with an afro hairdo and that was my meeting with Stan Prusiner and we did quite a bit of work with him doing mouse bioassays.

Interviewer: So what did he come specifically to do? It sounds like he had a plan even before he came.

WH: Well he was – wanted some of his fractions titrated for infectivity.

Interviewer: Right so this was when he was working on purifying – he was already working on purifying the agent –

WH: Yeah this was before the prion –

Interviewer: And he needed a place to bioassay?

WH: That's right. That was it. And then I visited him in San Francisco and he eventually ended up a mouse base at a Naval Installation in Oakland and we went out there and looked at and it wasn't as extensive as what we had here for him. And then, of course, he's gone way beyond. I haven' t seen Stan for quite a while. The last time he – I don't know when was the last time I saw him. Maybe it was the last time that I saw him was in '80 – was in '90 in Brussels. There was a big meeting there on TSEs and I gave a paper on scrapie and just to rile him I used the term scrapie virus and he took me aside right after the meeting and said, "I've got to talk to you about that." So we had breakfast the next morning and I was asked to revise my nomenclature. It wasn't a virus it was prion.

Interviewer: Really he asked you to do that personally?

WH: Oh yeah. And then he used to call – I think I wrote him a letter and I got a nice response from him when he got his Nobel Prize in, what, ' 97. I always considered him a good friend and we just had never been in touch and certainly never talked science.

Interviewer: Were you interested in the work he was doing – the purification work?

WH: Yeah we were in on part of it, but then he got beyond that into all the biochemistry when the work we were doing for him was shut down that was the end of it. That was shut down in April of '78.

Interviewer: When did IHC –

WH: The whole thing was shut down.

Interviewer: When did immunohistochemistry prion protein start about…?

WH: Oh actually I don't know.

Interviewer: Was that before or after the facilities were shutdown?

WH: Oh that was long after.[See UPI Science News July 30, 2004]

Interviewer: Long after.

WH: Oh yeah.

Interviewer: So it wasn't until after – so what did you do after the facilities were shutdown here?

WH: I just played pathologist.

Interviewer: You played pathologist to other –

WH: I looked at a lot of old mink and got a few papers out on straight mink pathology.

Interviewer: Did you ever do immunohistochemistry and how do you think that changed the field, I mean, in terms of doing sort of diagnosis of pathology?

WH: Yeah it has certainly been a valuable tool in establishing a diagnosis when it's applied properly. I have had no experience with it, but I have the impression, now, well it's the way things are. It's used to confirm a diagnosis or the presence of say BSE or scrapie and you don't have to look at the brain. You don't know what the lesions are like really, because you can get –

Interviewer: Is that a problem or not and what do you think we might be missing by not looking at the brain more carefully?

WH: Well the little I know about the immunohistochemistry is that in itself, maybe it depends upon the antibody, and if it isn't specific for all of the TSEs you're going to light it up and admittedly they've been using the pattern, again a profile, what areas of the brain light and whether it is neuronal, whether it is astrocytic or whether it's out in the neuropil to arrive at some distinction of – and in scrapie they thought it might be the basis for distinguishing strains of the agent in one of the recent papers that I haven't seen.

Interviewer: Jeffery.

WH: Well in the surveillance programs, which includes ours in the U.S., all they have to do as far as BSE, all they have to do is take out the caudle [?] part of the brain stem and the medulla, fish that out through the [unintelligible], do the section and get whatever pieces of brain you need. And so it lights up and they've found it in Japan and then there's some little difference in the pattern of the staining and they immediately conclude that it is another strain. So I asked Gerald, "Well what did the Japanese find as far as the lesions in the brain?" Well it wasn't available. So –

Interviewer: Had they thrown the brain away? Had the brain –

WH: Oh they don't just take – they never take it out, no. That's true here too when all these animals – they're not going to take the brain out, one in Britain too. It's expensive taking a brain out, because they've been taking the brain out and probably it's –

Interviewer: Scooping through the foramen magnum is much less arduous than cutting – then sawing the skull open.

WH: Yeah. You often get the medulla is sticking out here and maybe a piece of cord on it, and you take something like a snare, wire snare, or a grapefruit cutter, reach up in there and cut off the cranial nerves, maybe I don't know how far they go, or maybe up to the pons – just ahead of the pons, cut out the cerebellar [unintelligible] and pull it out.

Interviewer: How much of this do you think is just done for ease of technique rather than what would really be most helpful in terms of if you really wanted to do surveillance for, especially if there were other forms of BSE –

WH: Well they'll miss it. They'll miss it. Oh and there was this paper that came out of Italy two cows, rather old cows, neither one showing clinical signs one 15, one 11, I guess, and they found there was very little spongiform change but what was present was higher up in the brain the immune-histochemical – the chemistry staining was higher up in the brain. Well and this was associated with amyloid plaques and so they concluded they have a second strain of BSE. Well it's not BSE; it is another TSE.

Interviewer: It's something different.

WH: Yeah. Well I think they're missing a lot. I had a good chat with Gerald Wells about a week ago about this and I guess we just ended up disagreeing. It had to do with the staining and I said, "All right, I'm of the old school. When I took neuropathology you had to know the topographic distribution of the lesion because in those days we didn't have all the ancillary techniques to arrive at a diagnosis and you could distinguish this disease from that disease on the profile of the topographic pattern of the lesion." That was especially true in some of the inflammatory – some of the encephalitis cases. I said, "You make too much of this immunohistochemistry staining as far as understanding the disease. So you've got a different pattern, but do you equate the site of staining as a lesion?" I got the impression that he didn't and I said, "Oh I don't buy that Gerald, because you can have lesions without staining and you can have staining with out the usual lesions." I want to see the lesions. Well I may be all wrong, but that's the way I look at it and that's when it came up, "Well nobody does that anymore. It's just too expensive." I said, "Well that's part of it. The other part it nobody has the training or the willingness or the experience to do it." You have to know some neural anatomy to do it to begin with and sure it's tedious, but I always found it fun. If you're going through and you're identifying parts of the brain, nuclei but you have to have a roadmap, that helps, but you have to have some experience too and there are few people doing it. Few people doing it for those reasons I think. It may be harsh judgment but I think it's for that. It's costly and everything is so different, but Gerald said, "What do you want them to do cut those brains the way you looked at them ten years ago, 14 years ago? It's 150 pounds. That's just cutting them."

Interviewer: Just cutting them. That's not the labor of…

WH: Looking at them.

Interviewer: Staining them and looking at them.

WH: Well that's you know preparing the slides. It's not having someone actually do –

Interviewer: A skilled person do –

WH: The examination.

Interviewer: Examining, yeah. So and then – but when considering again the triad and sort of relating that nosology and how these different waves of nosology have come about.

WH: Well I think early on you didn't talk about TSEs before – well you didn't talk about them in 1958, and it was only later when Gibbs and Gajdusek put Kuru and Creutzfeldt–Jakob disease in chimps and they saw all this spongiform change that they came up with the idea. I think originally it was probably sub-acute spongiform and then they settled on transmissible spongiforms, and then that whole story evolved with bringing Creutzfeldt-Jakob disease in along with Kuru so you had two examples of scrapie like disease. Then you've got TME, and then Chronic Wasting Disease comes along and then BSE, so you got all those TSE. Well, as far as the so-called triad, early on I never saw much spongiform changes actually in any of the sheep I looked at here from [unintelligible], naturally infected Suffolk sheep.

Interviewer: Had you seen it in Compton or not?

WH: I looked at a lot of it in – oh in Compton? They didn't pay much attention to it. Way back then we never thought about it even old Israel Zlotnik. He was the first one to even mention it that he had seen – I don't know what they call it spongiform change or vacuolation – that he had seen that and wasn't all that impressed.

Interviewer: I just want to make sure I'm getting the terminology correct here because there is two things, there's vacuolation of the neuropil and then there's vacuolation of the pericardium right?

WH: The pericardium.

Interviewer: And those are two different things? So the thing that was being overlooked was the vacuolation of the neuropil, which is called the spongiform change right? So that no one was paying attention to that. Were people paying attention to the vacuolation in the neurons?

WH: Oh yeah, that was the basis for the diagnosis of scrapie.

Interviewer: Okay.

WH: [Break in audio—picking up interview in middle of question]… died a couple of years of ago, he had Alzheimer's disease and he was 90, but he was a great guy. You could tell him some pretty raunchy jokes and he'd have one to counter it. He was great. Gordon and Pattison, they may have been still at Edinburgh when they wrote that paper. That was one that everybody referred to.

Interviewer: Right and that was the vacuolation in the neurons –

WH: Yeah.

Interviewer: The main feature. Now what about astrocytosis at that time was that something remarked on?

WH: No that was completely overlooked. I think, again, that impressed me when I looked at the goats and it was new to me with all that I read about scrapie, they'd never mentioned it. Zlotnik, who was always doing his marathon on [unintelligible] and nerve cells.

Interviewer: What did these people say when you brought the astrocytosis to their attention like Zlotnik or –

WH: Oh well, he actually mentioned it then. I don't know if whether it was before or after we talked about it, but he mentions it in one of his papers. A later paper… some of his earlier papers in the early '60s were all on vacuolation of neurons, of the pericardium, but what everybody missed, and how I got onto it I'm not sure, except that went I went to Compton the USDA gave me a lot of titles of papers, of foreign papers, and some of them were translated from the foreign language. I'm not sure whether I got the entire paper translated. I may have, but it was published in 1937 in France, Ivan Bertrand, he was the M.D. neuropathologist. I have a book down there that he wrote that I was going to use to learn French and two veterinarians –

Interviewer: Don't worry – don't worry about –

WH: They reported – I was reading the best report on the pathology of scrapie that occurred. All these other people just had been preoccupied with these neurons with holes in them, Brownlee [?] and way back to when they were first reported by Besnoit and Morel in 1898, but Bertrand pointed out that there was a distinct astrocytosis then. My feeling is that in neuronal changes you have difficulty separating them from artifact or postmortem change and whatnot and significance might be equivocal, follow them and you got a good astrocytosis. That was evidence that something was going on. They were the whistleblower in the neighborhood. And so that was missed and, of course, Parry missed it until Elizabeth Beck joined up with him. She was a German neuropathologist working with him at Oxford and got him straightened out on the muscle thing and she reported the astrocytosis I think.

Interviewer: Did you have the pleasure of working with her? Like did you know her?

WH: I knew her, yeah, and we had good rapport. I had good rapport old Herbert Buckler Parry. You know, he was treated quite unfairly in Britain following the muscle fiasco. They never let him forget.

Interviewer: So he made one critical mistake?

WH: Yeah and then that was –

Interviewer: Tell me what the reaction was like.

WH: Well there were really a couple of reasons. One was this paper that came out in 19 – what the heck was it '56? – stating that scrapie myopathy likened to muscular dystrophy. It's a hereditary disease to begin with and nothing to do with these nervous system and all these holes you see in nerve cells that's a lot of nonsense. It's all muscle. Well, that was a blow to the people that had been working on it for years like Pattison and Stan and all of them. So they're going to shoot that down in a hurry. Tom Mullin [spelled phonetically] who was a veterinary pathologist from [unintelligible] he was working in Edinburgh when I was at Compton, working up there with Stan, and they put him on the muscle right away and, of course, he showed that you might get some muscle but it's not the myopathy. And then the fact that he was so adamant that it was an out and out hereditary disease, had nothing to do with a transmissible agent. And the stuff you produce experimentally, that's different, and I don't think he ever had a chance to review the data we had to see how we might respond, because we weren't working on experimental – the experimental disease. These were naturally infected sheep. This was what we found and it was transmissible to mice as far as the agent and we didn't find lesions in muscle. So – but he had the confidence of all the Suffolk breeders so he had a lot of information and I don't know how it's viewed today. I think – oh I don't how he pardoned the name of James but he was always called James Parry, H.B. Parry, James Parry, but his idea of it being a hereditary disease at least drew attention to the importance to the genetic background of the animal in reference to its susceptibility and that's the way it's looked upon now. Of course Dickinson, Alan Dickinson he would be one to be right there to tear him apart and that's way Alan – I haven't seen Alan for a while but yeah that's the way Alan is.

Interviewer: And Alan wasn't quite at Moredun, right he was somewhere else, but he was in Edinburgh is that correct? He was at the ARC? No wait I'm confused. I always forget what exactly was –

WH: The neural pathogenesis unit.

Interviewer: The N.P.

WH: Yeah that's where I last saw him –

Interviewer: He was at the N.P.

WH: Hugh Fraser was up there and Richard Kimberlin had been ousted – I don't know what the circumstances were from Compton. He came there of course after I left.

Interviewer: You don't know why he was ousted?

WH: No I don't know why he left. Anyway he wound up at this neural pathogenesis unit. Dickinson was running it and he wouldn't give him anything to do. So he was just sitting then put in his time and writing some papers and he wasn't even allowed into the mouse room. Dickinson was kind of eccentric, a little odd. I had dinner with him one night. We had a meeting out at – it must have been out at Reagents, well we had a hotel out at Reagents Park, I think, and we were staying there. It was a rainy night and he was going to catch the train to Edinburgh after the meeting and he had a base vile – whatever you call it, case that he was going to take to his daughter. I don't where he picked it up, but he had some special mice in there. I don' t know how he was keeping them from suffocating, but anyway we had dinner together because it was raining and nobody went out and that was the one time we really had a good time, didn't agree on hardly anything, but I had a good time with old Alan.

Interviewer: He was sitting there with a –

WH: He was as eccentric as –

Interviewer: Full of mice?

WH: In with the valise. He was a strange man. I used to kid him I said – we never had difficulty demonstrating scrapie agent in the brain of sheep, naturally infected sheep. "Well, it didn't work all that right." I said, "Well maybe it's the mouse strain, but we're just using this tough old mouse, but you have to have them live at least two years if they don't they're not good, because your titrations run out. It takes a year before the 10^{-1} gets sick," and "We have negative –" I said, "What are you using for brain and what's your inoculum?"

Interviewer: This is Alan Dickinson?

WH: Yeah. He said, "Take a little bit of the cerebrum." I said, "Yeah you take the calvaria off, there it is. You scoop out a little. That's it." You don't have to muck around with it and maybe you got it contaminated, and that's the worst place to get the agent. The titer is lowest there. You're going to miss it, because you want to get brain stem or cerebellar cortex. So we jousted a little bit over that.

Interviewer: That's great, but he was helpful in figuring out some of that, the importance of the genetic background.

WH: Oh yeah he's got a good background there yeah.

Interviewer: That was incredible, actually, that he pulled all that out.

WH: He did a lot of it – not it doesn't detract from –

Interviewer: No, no of course I understand he's a strange guy –

WH: He's just personally he's an eccentric little bugger and the last – I had a letter from him. Where the devil was he? He's somewhere down in England – I got a letter from him. I could find his address I guess from someone.

Interviewer: I think he's in Edinburgh still.

WH: Oh is he back up in Edinburgh now?

Interviewer: Yeah.

WH: Oh, I lost track of him. The old timer that I know over there that was there when we lived in Compton is Alex Mackenzie, he wrote one paper on the histo-chemistry of scrapie and he got his doctorate at Reading.

Interviewer: Okay he was one of the ones who was there when you were there, but who –

WH: And he'd just come down from Glasgow and he was a good friend of my wife and I, and he's still a good friend, old Alex. Every now and then I get a call, I don't know what time he's calling, but it's late here. "This is Alex." It takes me a while the first time I hear the Scottish dialect. He's retired. He's still living in Compton. He raises black labs and judges shows.

Interviewer: Interesting. That's so interesting. Oh, Dick Marsh.

WH: Oh Dick Marsh.

Interviewer: Yeah if you could tell me – so we started out, we did the beginning of the TME story, and then when did you first get to know Dick Marsh and how did he…?

WH: Right here. Dick Marsh came in – let's see I did the mink in 1963, it must have been about '65 maybe. He came in with Helene and two of his children. They were sitting right here, right here and he was doing his graduate work and I don't know how much training he's ever had in pathology neuron histopathology. I think his background was mainly virology, but he was doing his doctoral dissertation on TME and we talked about that and I think talking to me, I think, was mainly about the lesions and how to interpret some of the changes, that was it. So from then on we were good friends – colleagues.

Interviewer: So he came all the way out here to talk to you about it?

WH: Yeah, but –

Interviewer: With his family?

WH: But probably he was on his way home in Oregon where he grew up. His dad was mink rancher.

Interviewer: That's fascinating.

WH: Yeah a mink rancher.

Interviewer: Is that how he got interested in the disease?

WH: I don't know how Dick got – how he wound up at Wisconsin and how he got interested in the mink disease. Whether that was – that may have been the first mink disease you know I suppose with his background and I think his background in virology with – and he was looking for a problem for his dissertation. That's probably why he did it. I don't know. I'd have to read his – I've got a copy of his dissertation.

Interviewer: Wow and then how did you keep in contact with him after that?

WH: Well it was usually at meetings. I don't think we ever really – well we corresponded now and then and I've got – he'd send out some material that I wanted to look at and sometimes he'd send it out for my opinion, brain material from mink usually – yeah mink, and what I wanted to get was something more recent and unfortunately it didn't last. I talked with him about – shortly before he died. He was at home. He knew what was going on, days were numbered, but we would see one another at meetings, TSE meetings, scrapie meetings and then had kind of a loose correspondence and –

Interviewer: But you just always liked him. Like he was a really – well how would you describe him? Like what was – was he very thoughtful or I mean…?

WH: Very likable person, yes very likable, very helpful. He was a person that was – he could get riled up, get riled up, and then he'd almost stutter, and he was so firm in his convictions, which was fine. He was a valued colleague and a good friend. He and – my wife and I always kept up with Dick and Helene at Christmas time and she called me, oh when was it, a couple of months ago I guess. She was out visiting her daughter who lives in Missoula. She was one of the little girls that was sitting here I think, DeDe and she didn't make it up to Hamilton and I had something going on and I couldn't get down to see her, but she came up maybe two years ago and we had lunch here in Hamilton. That was the last time I saw her.

Interviewer: Oh that's nice.

WH: We keep in touch at Christmas time. Now Dick was a good friend and there are few of those people like that, that you felt close too. Dick Marsh is one. I probably felt closer to him than any of the others that I've worked with professionally in this field. John Gorham over at Pullman I've known him for 50 years or more and he's a strange setup. He worked for the USDA and running this fur animal disease lab at Washington State University and he's kind of treated as part of the academic scene, but he's retired, but he still has an office there and he's always sending me something or calling me about something. This was John, you could just feel him calling through the phone line. He was always so excited about something.

Interviewer: What has your relationship been like with the USDA over the years like have you participated in work that they needed done?

WH: I had a good relationship early on when I was with USDA, Howard Johnson was my boss. He was in Beltsville. I was in Compton. The man that sent me the checks was in Amsterdam, well I didn't see anyone. Every now and then they would send someone over.

Interviewer: To check –

WH: I don't know whether they wanted to see if I was still there. They didn't bother me, they didn't bother me and they supported me. I needed a new microscope and I spent money getting some good photomicrographs at the National Hospital in Queens Square working with that fellow. Did it on old glass negatives, which I still have, they were beautiful, and things like that. But then, when I came I had to deal with them about scrapie and of course you get into the bureaucrats and the guys that have to do these regulations; I never did kind of warm up to those guys. It was just something that I had to put up with. But then, when we wanted to – well, when we came over on this tour in '59 I mentioned that one of the USDA members, Jim Hourrigan who was in charge of the scrapie eradication program; when we wanted to collect some material from naturally infected sheep in those days they took them all down to Mission, Texas. If they didn't kill the whole flock they would confiscate the whole flock – well certain flocks and take them down there and then put them under observation, but it was a great place because they always had sheep affected with scrapie.

Interviewer: And who were the people who ran that?

WH: Well that was USDA and it was under Hourrigan. It was down on an old Moore [?] airbase, because we used to sit there, have coffee on this big table where they folded parachutes, and that was another experience, too, when we went down. I was trying to remember when we first went down. Anyway Jim Hourriganwas the contact man, and he gave me a booklet that I could use to buy tickets and all that sort of stuff.

Interviewer: You mean to go back and forth to Mission, Texas?

WH: Yeah to Mission, Texas. Well, after a while, I don't know when that ran out and I said, "Well USDA – Rocky Mountain Lab will pick it up, because this is an important study."

Interviewer: And this is the natural Suffolk pathogenesis study that you were working on –

WH: Yes.

Interviewer: That you were working on with them? Okay.

WH: Yeah and we should have – I had too much going on here in what we were doing, Aleutian disease, TME, we did a little work on progressive pneumonia and I had too much going. We should have taken advantage of that opportunity there, and what existed here, and exploited it a little more, but anyway Dick Kennedy and I used to go down there. I think we started about, I don't know, maybe it was '68 and we just wanted to collect material from naturally infected sheep, but it would take two days to get there. We'd have to fly to Dallas, hold them up there, and then take that trans-Texas flight with these cowboys that fly into McAllen, Texas, and Wilbur Clark was the resident director of that scrapie field trial. Wilbur is now the federal veterinarian in Helena, Montana, but he was a great fellow to work with and he had quite a crew. That was quite an experience. Anyway, Dick and I would go down there. We sent down all kinds of things – our own guard, all the equipment we needed and then we'd leave it there and we had a marathon. They didn't have a decent necropsy room. I think I had to move guinea pigs out and clean the table off of guinea pig feces and things like that – better get organized. They just weren't prepared for what we did. We had already cut up the sheep.

Interviewer: They didn't have a place to do postmortems?

WH: No.

Interviewer: Like that.

WH: Not the way we did it.

Interviewer: Okay.

WH: They cut them up the way I did. We really took them apart and you had to them in a way that – and Dick was a great fellow to work with. So we had quite a team. So we'd go through these sheep. Well you'd bring them in and you'd have to knock them out, get some cerebral spinal fluid, hang them up, skin them and then collect what you wanted and then they'd get rid of the carcasses. They had an old flamethrower out there, throw them on a pile and hit them with the flamethrower. It was primitive stuff down there.

Interviewer: That's amazing.

WH: That would be quite a story if I were to recount all the details. Well we did that several – quite a few times, collecting material, and then when we wanted to collect specimens from normal sheep these nice, beautiful lambs, 10 – 12 months old, "Well, I don't want to part with them." I said, "Well, we've got to have some Jim and Wilbur. You're just going to have to part with them."

Interviewer: You mean they bonded with them or did they…?

WH: No they could sell them.

Interviewer: Oh, wait but they were potentially scrapie.

WH: Yeah. I don't know whether they wanted them for meat. I think that what – really they wanted to keep them as breeders, because they had this long-term study on the – well the in-flock transmission or what the prevalence might be in some of these flocks and that was disturbing their numbers. I think that was the real reason. Well they wouldn't be selling any off of there. But we got the material and they went out on the flamethrower pile too. But then they had a fellow down and old Texan character. I remember the first day we went there we were, Dick and I were dressed in jackets, got off the plane, he took us out to Mission which is about 28 miles away, where they had the scrapie field trial at the small airbase and was taking us around through this rattlesnake infested area, and he called to this fellow D.C. Bruce. He got – he introduced a couple of fellows. He said, "What do you got there, a couple of GSA teams out of Washington?" You know all dressed up and figured where coming there to study scrapie. Anyway he was good with a welding torch. He made a nice table for us, a cradle –

Interviewer: Oh so he made you a place to do the necropsies?

WH: He made a table and a cradle and we could put these animals in the way we used to do it here to anesthetize them and no fussing around and, well, I think we used it as the cradle lasso to put the carcass on eventually when we opened it up. That worked out fine. Anyway he was good with a welding torch but I think in those days he and Dick had to seal some of these ampules with his welding torch that I did on the TMEs and then the – to make a long story short we'd have all this brain material in these vials in dry ice and not have stuff in formalin and some in formalin ammonium bromide, so I got a good [unintelligible]. We had them in boxes and we took them right into the airport. Sitting there with sealed – and we got by with that for quite a few years until the last time – it may have been the last time some seasoned flight attendant, an older person, said, "You can't you do that. You're going to have to check it." Well we didn't want to let all that valuable stuff out of our hands but anyway that was the end –

Interviewer: Of course not, did you check it?

WH: That was the end of it.

Interviewer: Yeah that was the end and then after of that then did you ship it?

WH: We had to pack it a little differently and ship it.

Interviewer: Yeah, yeah. So the USDA was really helpful in terms of assisting you with getting material. They provided – they were – they had this heard this scrapie flock and you could go down and get material, and they even helped for a little while paying for some of your flights out there. Did they ever fund some of those research projects?

WH: Not here. They couldn't do that anyway, but we had great cooperation.

Interviewer: Were they interested in the results?

WH: Well Jim Hourriganwas I don't know as I always told Jim – told others – I had this very amicable relationship with USDA because I didn't have to deal high up. I dealt –

Interviewer: You dealt with Jim.

WH: Jim Hourrigan and from there down and he had a fellow working with him Al Klingsporn now he's in Rochester, Minnesota. He's retired. He was usually there. Jim usually wasn't there, but Al Klingsporn would come down, and then Wilbur and his crew, they were most helpful. So everything was laid out when we went down there. Once they knew what we were up too, we weren't just a couple of GSA teams out of Washington.

Interviewer: Did you stop wearing your suits to go down?

WH: I don't know what it was, but anyway that was old D.C. We had a great time. Always had a good time down there, but the equipment was primitive. It took us forever to autoclave at the end of day and to get –

Interviewer: You would autoclave down there?

WH: Yeah on all of our instruments.

Interviewer: But they had really primitive autoclaves?

WH: It was primitive yeah. It just took a while for the thing to get cranked up.

Interviewer: What ever happened to that facility in Mission, Texas?

WH: I'm not sure whether it still exists. There's a woman veterinarian by the name of Sutton [spelled phonetically] that was running it there for a while, but I don't know if they had any sheep there. Wilbur did some experiments and then Gibbs and Gajdusek took animals or used animals down there, which was just a mistake.

Interviewer: Why?

WH: Well they inoculated them with Kuru and with Creutzfeldt. Well they're outside which is all right down in that country, but I don't think it – it just – I think compromised – in my view compromised the whole thing if you got a positive. I don't think the isolation was that good. You just had to assume the whole bloody place was contaminated with a scrapie agent. So I – the relationship – I still keep in touch with Jim Hourrigan. He lives in Vienna, Virginia and he calls me periodically and he sends me some things, and Wilbur Clark, he is up in Helena, the last work we did together – when we were going down there, and this was before BSE hit the scene, I always told Jim Hourrigan and Wilbur, especially Wilbur, you have to inoculate some cattle just to see what the host range is for cattle or just run some – these – bring them calves in here with your sheep, see what –

Interviewer: How long ago was this that you were suggesting that?

WH: Oh that was…maybe late '60s.

Interviewer: Okay.

WH: And nothing ever happened. Well then it must have been after we discontinued going down there – that must have been – they did inoculate some calves and 10 calves, 3 of them came down with clinical disease, and this was mainly some instability and then becoming recumbent and they – he sent me the brains from two. The brain went to somebody in USDA and I never saw much. So there was always a question of well did anything really happen? And there was never a formal paper, certainly on the pathology, they talked about it clinically and Wilbur had a couple of little papers for some journal I guess and…well nothing came of it. There was always a question, but whether anything happened when you put scrapie agent into the cattle and this was before Cutlett [spelled phonetically] did anything on animals. So I was talking with Gerald Wells well it was when Gerald stayed with me in the spring of '89. He stayed with me for a week.

[Audio break picking up in mid-sentence]"…brains from remission, cattle brains and what did you see?" "Well," I said, "I've forgotten, I didn't see much." I had the section somewhere and I've got all this material in the lock-up, north end of town and I didn't know what I was going to do with it – 50 years of stuff; sections, paraffin blots. Anyway, went down there and found these sections, came back here and looked at them. And he says, "You'd better make a complete study?" So I did. Finally got all the information from Gerald – from Wilbur, and Joe Gibbs had written something about it but he had misinformation. They used several different sources of the inoculate. Anyway, I got that all straightened out, I looked at videos of the clinical picture, went and spent a whole afternoon with Wilbur questioning him about the clinical picture – so I got that whole story. I looked at the sections and then I got in touch with the man at USDA, I said, "Send me all your material on this other animal." Well, we finally got the paper together and then I tried to get published and, well I didn't look at controls. I said, "Well I know what a normal cow's supposed to – what it should have in its brain or when there's something there that shouldn't be there." Well, nobody would buy that. Finally, I sent it to the American Journal of Veterinary Research, and I think Dick Marsh was the referee, and he said, "Publish the thing. Hadlow knows what he's talking about."

Interviewer: Right, yeah.

WH: So I got it published.

Interviewer: Finally!

WH: And then, as it turned out, when Cutlett [spelled phonetically] wrote his paper, I don't know if it was before or after, he didn't find much, but he didn't look as hard as I did, I guess. And I even used the old [unintelligible], and that showed up a few things.

Interviewer: What did you find?

WH: I found some very sparse spongiform change and some neuronal change, a few – frontal neuronal change that I'd always associated with scrapie, they'd become dark and shrunken – a few cells, a few of the neurons, had vacuoles in them where you'd expect them, in the medulla, and you always find them in the red nucleus in cattle anyway. And then some astrocytic response.

Interviewer: Mmm-hmm. So you found everything – little bits –

WH: Mmm-hmm, little bits of everything. And it was consistent with – these were animals that were showing clinical signs and it was just an illustration of how subtle the ordinary histological changes might be–

Interviewer: Oh that's amazing how easily you could miss that.

WH: Because Dick – or Reynold Cutlett [?] found very little in his cattle but I don't think he looked at all the parts of the brain that I did, because I had the whole brain and got those cattle – those were cut up before I retired. So I've got the blots here somewhere.

Interviewer: But so this was something that even you had to look pretty hard to find the pathological evidence, but it was there. It required –

WH: Mmm-hmm. But having done this regularly, it lights up right away – "This isn't right." That's part of the experience.

Interviewer: Oh, so can we talk a little bit about artifacts that can look something like spongiform change or vacuolation in neurons and how – if we talk about what can cause them, why they're mistaken and what you can do to differentiate the artifact.

WH: I don't know whether I can be of much help there. As far as vacuolated neurons, I always have taken that as a real change. Except maybe in the Purkinje cells of the cerebellar cortex. Sometimes I think it's more of an expression of postmortem change. As far as spongiform change, all that's limited to gray matter. We can distinguish that from holes in white matter. I never felt that I had any big problem in distinguishing a real spongiform change from artifact. Neuronal changes you have problems, and there were a number of early papers from a fellow by the name of [Harry Meyer?] from NIH, who concluded that much of what has been described as neuronal changes are in fact artifacts. Now that may be so, but the sort of change that I saw in scrapie – this was in well-fixed, freshly fixed brain where I think the conditions for favorable fixation were present. But I always found that – never thought that most of it was artifact. The individual cell, there might be some question there.

Interviewer: But not – see, now here you're talking about your own skills. But what about other people – other people looking at these tissues, what are some of the mistakes that people can make when looking at these things?

WH: Well I don't know, I've mentioned that these days someone finding some vacuolated neurons in the medulla of an animal might jump to the conclusion that he has another TSE. And you just have to understand that all of these animals have some vacuolated neurons –

Interviewer: Especially with aging, right? Isn't that something –

WH: I don't know whether it's necessarily associated with aging, but a fellow sent me some sections from possum; he was concerned about that. Well, in the end he went through the whole business of checking in for prion protein and immunohistochemistry, it was all negative, and I don't know whether he ever tried any infectivity studies but concluded that it was just one of the things that occurs in the possums, I don't know. If it has other significance, see them in cattle, as I say, in the Redmond case, seem them in the sheep and the dorsal motor nucleus of the vagus and not many that you see have scrapie. Mink you don't see them, even with TME; very rare. I suppose if I had one comment to make about examining the brain, is they're never thorough enough. And material that's to sent me, I suppose I'll attribute this to Hadlow. He always says, "Don't send me those cheese-pairing bits of brain that takes you half an afternoon to figure out where you are, if you have enough landmarks in the section." They sent me some hog – sections of hog brain, market hog, a number of years ago that created quite a stir. Someone found vacuolated neurons.

Interviewer: Do you remember around what year this was?

WH: It got on the Internet, my report, because some reporter or attorney asked – I said, "Well, that's confidential, [unintelligible]." "Well I can get it under the Freedom of Information." Next day it was up there. So that was all right. That was…oh God, three, four years ago. I had this – letters there somewhere. But I had a lot of phone calls. Yeah, because it hit the newswire and all these reporters were calling, and they thought they had another big story and – TSE and these market hogs. And these consumer advocacy groups, they always get hot on that. Well anyway, I sent them my report I found two vacuolated neurons, something else that I said I might be suggestive, but there certainly wasn't any clear cut evidence of a scrapie-like disease. And I think I pointed out that you find vacuolated neurons in swine as you do in [unintelligible]. And I did eventually identify where I was, I was in the [unintelligible] medulla because I could see the area most extreme sticking up – that's the one thing I could identify.

But I think that was – from the experience I had, they're not thorough enough. And working with these young fellows that worked in England, there's a number of young fellows when I was there, I was supposed to be studying these cow brains but I looked at piles of sheep and goat brain for Jim Wood, he wrote some good papers. "Come over and look at this" – "Well, the first thing they've got too much power. And too much light!" I'd always tell him, "Start out with the handlings, figure out where you are, and then start at low power. Then scan them. You got to know where you are; you don't just take a piece of brains out right in the middle of sectioning a liver." And that's – well I don't think that's emphasized enough. And pathologists – veterinary pathologists get good training these days, but it's kind of a specialty, I guess. You have to have a bent toward it. They should understand that at least some of them you're working with the brain that one little section isn't going to do like it might for looking at a liver. And of course there would be a difference there too, but it's not as drastic as in the brain where every level is different, they respond differently. Astrocytes aren't the same all over the brain, things like that as well. That would be [unintelligible].

Interviewer: Right, right. Now, with the – okay. So the incubation – so all of those pathogenesis studies that you and Eklund did, you did titers to establish concentration –

WH: Based on endpoint dilution.

Interviewer: Based on endpoint dilution, and with the increasing use of the incubation time assay or the incubation period assay, is this to get at similar data, like when they're using that as a stand-in for a concentration of infectivity, as Kimberlin's done, Prusiner's done, other people have done, how does that affect the field?

WH: Well, as I say, if you're working with a strain of the agent that's adapted to a given system, animal system, I think that works. And a given inoculum, I think it's been demonstrated if you go from spleen to brain it might not apply. But in the end, even with a decimal dilution endpoint it's an escalation, whether you're using Reed Muench or Spearman-Karber method for calculating the endpoints. So no, I think in most instances that's certainly better than nothing because in too many instances infectivity hasn't been determined. Well we put in so much – well, so much what? What's the baseline? We can say at least when we inoculated animals we put in so many mouse LD50s [?].

Well at least it's a baseline, I don't know how it compares with a sheep or a goat LD50, but at least we have it as a reference point. I think that might be [unintelligible] some of the reason it worked on BSE – I talked with Gerald about that, although I think he understands, you've got to do decimal dilutions. But they don't do that really on BSE. We don't – that's the problem with so many of these – we don't have enough information on infectivity anymore, or the pattern of infectivity. And immune-histochemical staining and infectivity aren't the same, as far as I'm concerned.

Interviewer: What would you do, if you could? If you were still in the field right now and in your prime, what do you think most needs to be done in that area?

WH: Well, I wouldn't get support for it.

Interviewer: Well, don't worry about that, let's say you had infinite support.

WH: I would get more information on infectivity.

Interviewer: Of what? Of which animals, which types of –

WH: Any of them, any of – well scrapie, replicate some of the work we did in different breeds, because we had a little indication that breeds other than Suffolk – the pattern wasn't quite as nice, and not as uniform, whereas it was widespread in the Cheviot. There is a difference in the Cheviot; no one has pursued that. And much of the work that they've done in Britain – I offer this as a criticism, they haven't done any infectivity work. Put in so much in volume; well, that doesn't say anything.

WH: What do they need to do, or what should be done?

WH: Well, we need some good bioassay system. Whether that means we need to sit around and try to produce some transgenic mice, that may be the answer for some, but certainly it wasn't necessary for scrapie. And I think Gerald has been able to make whatever strain of mouse he's using work for BSE. Admittedly, things might happen sooner, that would be an advantage if it costs money. I would like to see more information on infectivity.

Interviewer: So you mean like the parts of the body?

WH: The distribution – that or the –

Interviewer: The distribution.

WH: Well why is – from the information we have, BSE is altogether different from scrapie. Its external distribution or replication is extremely limited, and I suppose for that reason – obviously for that reason it's not contagious, it's not shedding any, the way sheep do, the way deer do. But today, given the emphasis of trying to determine the true nature of the causative agent and all that involves, and all the laboratory artifacts with models, I would be – the whole time I would concentrate more on the disease in the natural host and try to learn more about the replication of the agent.

Interviewer: So doing like the types of – like the way that you did pathogenesis studies where there were multiple time points at regular intervals where you looked at lots of different tissue and you used a bioassay to titer infectivity; doing something like that on cattle, on deer, on some of these different – like you're saying even with scrapie, in some of these different breeds or even replicating what you've done with the Suffolk would be useful information. You think focusing on the natural host –

WH: Yeah, I would, I'm lost when it gets into all this biochemistry. But I think there are breed differences and the real significance of strains. Does that have a bearing on the pattern of external distribution, fundamental to the pathogenesis of the disease? How does the agent get to the central nervous system? That's where it does its damage. And then how all this would relate to the particular codon and how this relates to, or if it does, have any relationship to – well I know there's some relationship to an incubation period and clinical presentation, but also the pattern of lesions in the central nervous system, and nobody's really worked on that. It's disappointing, I suppose, nobody else really worries about it.

But the other concern about whether BSE agents had gotten into sheep, because when you put it in an experiment it comes out looking like scrapie, clinically. And then Foster [spelled phonetically], I think it was, reported from Edinburgh the lesions – says it looks like scrapie; well, yeah, but it's kind of a flimsy description. How extensive – did you look at this, did you look at that, and now they're concerned about it and whether some of these so-called cases of scrapie are occurring naturally in sheep might actually be caused by BSE.

Well, it takes a while to have a way to do it – they can do the mouse work and distinguish them, and then there are biochemists who do it – I guess with glycosylation or whatever they do it. But you might get some idea if you just get a better idea of what the lesions were like in the brain. I think it's a fairly – in my mind it's a well-established anatomical entity. There's more variation in the lesions of scrapie in sheep than there is in cattle, BSE, that's so stereotype that's monotonous. You've looked at one, you've looked at a hundred, they're all the same except for [unintelligible] up and down the road variations. But not like sheep. I was impressed with that because my experience here with the American Suffolk breed mainly – there were a few others but mainly the Suffolk, it was fairly straightforward and always the same. But I didn't see lesions in certain places – it didn't look proper. But when I looked at this material in England, a lot of this was from – well, I had some 80 breeds, but it was from a lot of breeds that I'd never examined. And then some of the foreign breeds – the Texel from Holland, and – I guess it probably came from France but two from France, the Charollais and the Bleu du Maine; their lesions are different, they're different. But it's scrapie.

Interviewer: What are they like?

WH: Well you get more high up and you get into –

Interviewer: More prefrontal cortex or –

WH: You get some in the prefrontal cortex and knock out the old [unintelligible] cell. Then some of them would even go back, not quite to the occipital but you might get some in the parietal. But anyway, there was sort of a pseudo laminar in the cerebral cortex, the neocortex, but then there was a variation in some of the other areas – cerebellum. Anyway, just you better appreciate the variation that they talk about, and this seemed to be breed related, and that may actually be strain related, I don't know. Those are things that would interest me, not that it's going to solve the problem but I think we'd know a little bit more about the disease. I don't know how much more we're going to know about the disease with the work that's being done. I haven't followed it that closely so I shouldn't say. But you know that – this is a side issue – the prion? It's not really a good acronym is it? It's actually a – I think you would call it a holograph – there is a word that exists in the dictionary, are you aware of it?

Interviewer: The bird?

WH: Yeah.

Interviewer: Yeah, yep.

WH: The prion.

Interviewer: Is that why everybody in Britain insists on calling it the prion?

WH: Oh, yeah I don't know how [unintelligible] but I had an old mouse geneticist point that out to me. Ocean going petros [spelled phonetically].

Interviewer: Okay, so when you were on this tour – I'm interested in this tour you went on in '59 with –

WH: Stamp, Gordon, Hourrigan and Sheehan [spelled phonetically].

Interviewer: Right. And where did you go exactly?

WH: Well, we started out in Washington, DC, I suppose at the USDA building. Then we went to Columbus, Ohio, met with sheepmen there –

Interviewer: So actual sheep farmers?

WH: Yeah. They made up the audience because they wanted to hear our spiel. Then we went to Chicago, I don't remember with whom we talked there, and then we went to Denver and had the usual mixed bag I guess, because it was publicized, and then wound up in San Francisco.

Interviewer: And what was the main goal?

WH: Well I think it was to inform the shepherds, sheepmen in this country, what scrapie is really like and the need for an eradication – or they called it eradication, but a control program, and to dispel some of the myths that grew up, some of it from James Parry's work I think, because he had somehow gotten in solid with the sheepmen in this country and was quoted in all these – like the shepherd/sheep magazine.

Interviewer: So they were all quoting Parry, they all liked his theory. You also mentioned that he was in pretty well with the shepherds in the UK –

WH: He did.

Interviewer: He had access to their data. And was it also because they liked his theory?

WH: Well I don't know about that. But he certainly had gained the confidence of the purebred Suffolk breeders in the UK, everybody admits that, and that was the source of all of his information. And his conclusions didn't fit the likings of others.

Interviewer: And then in the US though, it was more in a political context that his data got used.

WH: I think so. They were looking for ammunition to shoot down this USDA eradication program which was based on the premise that it's an infectious disease; it's not.

Interviewer: And then eventually the program was shut down.

WH: Well, it shot itself in the foot.

WH: How so?

Interviewer: Well, I don't remember the chronology of it, but so originally they took the flock, killed the whole flock – or certain flocks that take a commission…they were just taking the ewes and the offspring and some of the – well, that's where you knew it was going to fail because there were a lot of infected sheep left there. And then the bloodlines, there were bloodlines, they were emphasized. It was in that bloodline, those were the animals that were taken and the non-bloodline animals were kept. So I don't know how long that lasted but I think that was the last of the program that died on the vine. Now they have a new entirely different – I'm not familiar with the details of certification. I haven't paid any attention to it.

Interviewer: But it fizzled out.

WH: Yeah, I knew it wasn't going to work. And then, I think, by their own admission, some people in USDA said that it was flawed, that it just wouldn't work.

Interviewer: Right, and because the farmers weren't accepting it? Or because why –

WH: Oh I don't know about that, I don't know about the reception of death and the farmers. It just was scientifically flawed; it wasn't going to work.

Interviewer: They weren't going to be able to eradicate it, right?

WH: No, certainly not.

Interviewer: Can you say a little bit about the relationship or lack of or the correlation between clinical severity, infectivity and the severity of the neuropathology that you find in the specimens that you look at?

WH: Mmm-hmm. I think with most of these TSEs in animals, there's no good correlation between the – well, the duration of disease, which may be reflected in the clinical center, and the severity of the microscopic changes, so that in some of these instances where the clinical course is short, the lesions may be severe. And I've always looked upon that as the difference in the temple of the pathologic process, from one animal to another. So there's not a good correlation there and as far as infectivity, I don't think anyone has tried to make any association or correlation there. As far as, say, the amount of concentration of the agent in the brain, I've never looked at that but I doubt whether there's even a suggestion of some correlation there.

End of transcript